



Consommation et
Affaires commerciales Canada

Consumer and
Corporate Affairs Canada

Bureau des brevets

Patent Office

Ottawa, Canada
K1A 0C9

(21) (A1)	2,104,649
(22)	1993/08/23
(43)	1994/02/26

5,071,9/43

(51) INTL.CL.⁵ C07H-021/00; A61K-031/70

(19) (CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Antisense Compounds Complementary to HCV Genome

(72) Seki, Makoto - Japan ;
Honda, Yoshikazu - Japan ;
Yamada, Ei - Japan ;

(71) Same as inventor

(30) (JP) 248796/1992 1992/08/25
(JP) 42736/1993 1993/03/03

(57) 12 Claims

Notice: This application is as filed and may therefore contain an
incomplete specification.

Canada

CCA 3254 (10-92) 41 7530-21-936-3254

2104649

- 257 -

ABSTRACT

Antisense compounds which are complementary to a genome derived from hepatitis C virus (HCV) were provided. Because the antisense compounds of the present invention act specifically on mRNA of HCV and inhibits translation of HCV gene, they may be useful as an antiviral agent.

5.

Antisense Compounds Complementary To HCV Genome

The present invention relates to antisense compounds complementary to partial sequences of the genome of hepatitis C virus (referred to as "HCV" hereinafter), and particularly to antisense compounds having antiviral effects such as inhibitory actions on replication of HCV and/or expression of HCV gene products, and the like.

To date, A, B and D types of human hepatitis viruses were discovered and serological diagnoses for these viruses were established. However, it has been a problem that cryptogenic hepatitis still exists (Digestive Diseases and Sciences, 31 122S-132S, 1986; Seminars in Liver Diseases, 6, 56-66, 1986).

On the other hand, in the middle of 1970s, a specific diagnostic technology for detecting hepatitis A virus (HAV) and hepatitis B virus (HBV) was developed and put to practical use. As the result, it has gradually become apparent that most of hepatitis due to blood transfusion is caused by pathogens other than such viruses as HAV, HBV, and the like which grow in liver cells, and such hepatitis was designated as non-A, non-B hepatitis. In the United States, hepatitis occurs with the frequency of 1 to 10% after blood transfusion, and 90% or more of the cases are non-A, non-B hepatitis (Jikken Igaku, 8, 3, 15-18, 1990).

In Japan, hepatitis occurs with the frequency of 10 to 20% after blood transfusion (about 200,000 cases a year), and 95% of the cases were non-A, non-B hepatitis. In addition, 40 to 50% of about 300,000 cases of sporadic hepatitis, which occur every year, are also non-A, non-B hepatitis. Most of these cases, including non-A, non-B hepatitis prevalent only in one district, do not have clear routes of infection such as blood transfusion, but it is considered that they may have other infectious routes (Jikken Igaku, 8, 3, 13-14, 1990).

With respect to the non-A, non-B hepatitis virus which is a main cause of this hepatitis after blood transfusion, Chiron Corporation succeeded, in 1988, in obtaining its gene fragment by a method completely different from conventional methods for exploring viruses, and this virus was designated as hepatitis C virus (HCV). Subsequently, the sequence of whole genome of the structural and non-structural proteins of HCV were published by not only Chiron Corporation but also Shimotoya et al. in the National Cancer Center (Proc. Natl. Acad. Sci. USA, 87, 9524-9528, 1990) and Takamizawa et al. in Osaka University, Microorganism Research Institute (Journal of Virology, 65, 3, 1105-1113, 1991).

Chiron Corporation succeeded in the expression of fused protein in yeast, said fused protein having at the

C-terminal the polypeptide (363 residues) occurring in the region from NS3 to NS4, which is part of the non structural protein of HCV, and having at the N-terminal human superoxide dismutase (European Patent Publication No. A1 318216) and developing an ELISA (enzyme-linked immunosorbent assay) using the expressed recombinant antigen with collaboration with Ortho Corporation.

The Ministry of Health and Welfare in Japan approved in the first place in the world the use of a kit comprising an antigen useful for the detection of Anti-HCV antibody in order to screen the blood for transfusion and to assist diagnosis of hepatitis C. On the next day of the approval date (December 26, 1989), the Japanese Red Cross Society nation-widely started the screening of Anti-HCV antibody for blood from blood donors.

Although there are about 1,700,000 patients per year in Japan who receive blood transfusion, it is estimated that 12.3% of which caught hepatitis at the time before the introduction of this test reagent, while only about 3% caught hepatitis after the introduction. Thus, the number of hepatitis C patients (173,000) due to blood transfusion reduced to about one-fourth (The Asahi in Japan, the morning edition on May 2, 1991).

However, C100-3 clone which is a recombinant antigen and developed by Chiron Corporation lacks near 20%

2104649

- 4 -

homology, in terms of the nucleotide sequence and amino acid sequence, when compared with an antigen cloned in Japan. Accordingly, there is some possibility that Anti-HCV antibody can not be detected by the use of the Chiron kit. Further, it is described in various reports that there are other regions, (for example, part or most of the region of NS1, NS2, NS3, or NS5 according to the Chiron Corporation's nomenclature), which have only 70% or less homology. Accordingly, it is likely that there are test specimens which cannot be detected by the above-mentioned kit. In addition, there are considerable mutants in terms of genome sequence among HCV (European Patent Publication No. A1 518313). It is believed that such mutation is attributed to the fact that the virus genome consists of a single-strand RNA.

Once hepatitis C develops, it brings about acute hepatitis, chronic hepatitis, hepatocirrhosis, and cancer in high probability and kills the patients. Thus far, a reagent which can inhibit the expression and replication of HCV has not been discovered, and it is desired to develop a reagent which can cure the diseases associated with HCV.

On the other hand, interests in RNA (antisense RNA) and DNA (antisense DNA) having the sequence complementary to mRNA have currently increased. When existing in cells, an antisense RNA or DNA couples with a complementary mRNA

to inhibit the translation of the mRNA. As the result, the synthesis of the protein coded by the gene is inhibited. Accordingly, the application of this technology has been thought valuable for developing a drug which exerts its effect through direct action to genes. However, the application of the antisense technology to diseases caused by HCV has not yet been fully investigated.

As described above, it appears that the HCV genome is apt to mutate very easily. The mutation results in the generation of many HCV subtypes wherein various portions, including important sites determining the character of the virus-constituting protein as well as surface antigen are different from each other. Hepatitis C is believed to occur when a human is infected with one of these viruses, and the symptoms can somewhat differ depending on the type of viruses.

The present inventors have isolated from one patient seized with hepatitis C plural viruses which differ from each other in amino acid sequence and nucleotide sequence (European Patent Publication No. A1 518313). Accordingly, the inventors have found it very important to design antisense compounds against these HCV genomes by the use of the conserved regions of HCV genomes.

In order to develop an agent which alleviates the symptom of hepatitis C patients, an extensive study was

conducted. In the study, a HCV genome was taken independently and its cDNA was used to obtain a new antiviral agent against HCV in the procedure detailed below. As the result, the antisense compounds were
5 obtained, which can inhibit the growth and replication of HCV and the expression of HCV gene products.

Thus, the present invention provides an antisense compound having a sequence complementary to a base sequence which consists of 10-34 bases and is extracted from:

10 (i) 93 bases from thymine at position 107 to adenine at position 199,

(ii) 152 bases from adenine at position 250 to cytosine at position 401, or

15 (iii) 52 bases from cytosine at position 808 to adenine at position 859,

of the base sequence shown in SEQ ID NO: 1, which can inhibit the growth and replication of HCV and the expression of HCV gene products.

20 Selection of the antisense compounds having the sequence complementary to the partial sequence of HCV genome and the method for determining the inhibition of the expression of HCV gene products by the use of said antisense compounds are detailed below.

25 The HCV gene is believed to be composed of a single RNA strand. The protein encoded by the strand is first

expressed as a single polypeptide. The virus structural protein, RNA polymerase, protease, helicase, and the like are believed to be produced via processing of the single polypeptide. Accordingly, it seems that when the
5 production of the first single polypeptide is inhibited, the expression of viral protease and HCV replication with the aid of viral RNA polymerase do not occur. Thus, if the protein from HCV gene is not produced, HCV does not grow.

As the region which is used for designing the
10 antisense compounds of the present invention, the inventors selected the region which can inhibit the translation of the first single polypeptide which is a precursor of viral proteins. The protein positioned at the N-terminal of this precursor polypeptide is the core protein of HCV, which is
15 followed by E1 (envelope), E2 (NS1 or envelope 2), NS2, and the like.

The inhibitory activity of the antisense compounds of the invention may be determined by the following method.

An mRNA covering the range beginning from 5' end of HCV genome and ending at the middle of E2 is synthesized using T7 RNA polymerase (Strategene). The synthesized mRNA
20 is translated in an in vitro translation system using rabbit reticulocyte lysate (Promega) and canine microsomal membrane (Promega) in the presence of the antisense
25 compounds, and then the amount of the expressed core

protein is determined by immunoprecipitation assay with the Anti-HCV core antibody. Furthermore, recombinant vaccinia virus containing HCV gene from 5' end to at least core protein region can be used. After infecting human cell lines with the recombinant vaccinia virus, the cells are cultivated in the presence of the antisense compounds, and then the amount of the expressed core protein is determined by immunoprecipitation assay with the anti-HCV core antibody.

In the meanwhile, the HCV genome has a special translation system, which can also be found in poliovirus, etc. (Pelletier, J. et al., Nature, 334, 320-325, 1988), and IRES (Internal Ribosome Entry Site) region which exists within about 340 bases positioned at 5' side of HCV genome followed by the core protein of HCV (Tsukiyama - Kohara et al., J. of Virol., 66, 1476-1483, 1992), is responsible for the translation activity of this system. It is believed that tertiary structure is important to IRES function, and core protein is only translated correctly when the tertiary structure of IRES is correct. In the above-noted in vitro translation system, ORF (Open Reading Frame) existing in the 5' untranslated region of said about 340 bases is not substantially expressed as compared with the core protein, and therefore, the HCV-derived protein is believed to be expressed by the IRES activity. Accordingly, it is

preferable to try to find out antisense compounds capable of inhibiting the IRES activity or destroying the tertiary structure of IRES, which results in the inhibition of the expression of the core protein in in vitro translation system or cell assay system.

Usable antisense compounds include phosphorothioate types wherein the oxide atom, double bonded with the phosphorus atom in the phosphodiester moiety which links adjacent two deoxyribonucleosides phosphorothioate type wherein the oxide atom is substituted with a sulfur atom; phosphonate types wherein the sulfur atom is substituted with a methyl group; unsubstituted phosphonate types; α oligonucleoside types, and the like (Crooke, R M, Anticancer Drug Des., 6, 6, 606-646, 1991; Tidd, D. M., Anticancer Research, 10, 1169-1182, 1990). Compounds other than nucleoside derivatives may be used as long as they can form a hybrid with mRNA target. Further, all of the antisense compounds which were introduced by Chrissey, L A. et al. in Antisense Research and Development, 1, 65-113, 1991, are also usable.

It will be easily understood that preferable antisense compounds of the present invention are those which are resistant to DNase, and those which form a hybrid to degradate with RNase H activity in cells (Tidd, D M., Anticancer Research, 10, 1169-1182, 1990).

Further, in order to increase a hybrid-forming ability of the antisense compounds without significantly decreasing a decomposing activity of the antisense compounds per se, it is advisable to convert a few phosphodiester bonds present at 3' and 5' terminal to phosphorthioate type or methylphosphonate type, while phosphodiester bonds in the internal sequence are remained unmodified.

Although any antisense compounds which meet the above criteria are satisfactory, preferred antisense compounds are those having a sequence complementary to a base sequence which consists of 10-34 bases and which is extracted from:

(a) 54 bases from guanine at position 127 to guanine at position 180;

(b) 34 bases from adenine at position 284 to thymine at position 317; or

(c) 34 bases from cytosine at position 343 to cytosine at position 376.

(Note: Any base number used herein corresponds to that in SEQ ID NO: 1).

More preferred antisense compounds are those having a sequence complementary to one or more base sequences which are selected from the sequences listed in the following items (1)-(3).

(1) A base sequence which is included within 54 bases from guanine at position 127 to guanine at position 180, and which contains 16 bases from cytosine at position 131 to adenine at position 146, 7 bases from cytosine at position 147 to cytosine at position 153, 6 bases from cytosine at position 151 to cytosine at position 156, or 6 bases from cytosine at position 175 to guanine at position 180.

(2) A base sequence which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains 5 bases from guanine at position 285 to thymine at position 289, or 6 bases from thymine at position 309 to thymine at position 314.

(3) A base sequence which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains 5 bases from guanine at position 355 to adenine at position 359, or 5 bases from adenine at position 369 to guanine at position 373.

Above all, the antisense compounds which have a sequence complementary to one or more base sequences selected from the base sequences listed in the following items (4)-(13) are particularly preferred.

(4) A base sequence consisting of 16-24 bases which is included within 24 bases from guanine at position 127 to cytosine at position 150, and which contains at least 16

bases from cytosine at position 131 to adenine at position 146 (for example SEQ ID Nos: 2-26).

5 (5) A base sequence consisting of 15-30 bases which is included within 49 bases from guanine at position 127 to cytosine at position 175, and which contains at least 7 bases from cytosine at position 147 to cytosine at position 153 (for example SEQ ID Nos: 114-369).

10 (6) A base sequence consisting of 15-30 bases which is included within 31 bases from cytosine at position 150 to guanine at position 180, and which contains at least 6 bases from cytosine at position 151 to cytosine at position 156 (for example SEQ ID Nos: 27-38).

15 (7) A base sequence consisting of 15-30 bases which is included within 31 bases from cytosine at position 150 to guanine at position 180, and which contains at least 6 bases from cytosine at position 175 to guanine at position 180 (for example SEQ ID Nos: 38-43).

20 (8) A base sequence consisting of 15-33 bases which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains at least 5 bases from guanine at position 285 to thymine at position 289 (for example SEQ ID Nos: 44-49).

25 (9) A base sequence consisting of 15-33 bases which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains at least 6

bases from thymine at position 309 to thymine at position 314 (for example SEQ ID Nos: 50-58).

5 (10) A base sequence consisting of 15-30 bases which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains at least 5 bases from guanine at position 355 to adenine at position 359 (for example SEQ ID Nos: 59-99).

10 (11) A base sequence consisting of 15-30 bases which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains at least 5 bases from adenine at position 369 to guanine at position 373 (for example SEQ ID Nos: 71, 72, 78-80, 85-87, 91-93, and 97-105).

15 (12) A base sequence consisting of 15-26 bases which is included within 26 bases from thymine at position 351 to cytosine at position 376, and which contains at least 5 bases from guanine at position 355 to adenine at position 359 (for example SEQ ID Nos: 81-99)

20 (13) A base sequence consisting of 15-26 bases which is included within 26 bases from thymine at position 351 to cytosine at position 376, and which contains at least 5 bases from adenine at position 369 to guanine at position 373 (for example SEQ ID Nos: 85-87, 91-93, 97-105).

25 Examples of most preferred antisense compounds of the present invention include:

2104649

- 14 -

(14) if antisense compounds meet the criterion of the above item (6) or (7), then those which satisfy both criteria;

5 (15) if antisense compounds meet the criterion of the above item (8) or (9), then those which consists of 20 or less bases;

10 (16) if antisense compounds meet the criterion of the above item (10) or (11), then those complementary to a base sequence consisting of 15-26 bases which is included within 26 bases from thymine at position 351 to cytosine at position 376; and

(17) those which satisfy both criteria of the above items (10) and (11).

15 Further examples of the most preferred antisense compounds are:

20 (18) the compounds complementary to a base sequence consisting of 15-20 bases which is selected from 20 bases from cytosine at position 139 to guanine at position 158 (for example SEQ ID Nos: 244-249, 260-263, 275-277, 291, 292, 307);

(19) the compounds complementary to the base sequence consisting of 30 bases from cytosine at position 151 to guanine at position 180 (SEQ ID No: 38);

(20) the compounds complementary to the base sequence consisting of 20 bases from cytosine at position 131 to cytosine at position 150 (SEQ ID No: 6);

5 (21) the compounds complementary to the base sequence consisting of 19 bases from cytosine at position 141 to guanine at position 159 (SEQ ID No: 106);

(22) the compounds complementary to the base sequence consisting of 20 bases from guanine at position 355 to cytosine at position 374 (SEQ ID No: 98); and

10 (23) the compounds complementary to the base sequence consisting of 20 bases from thymine at position 353 to adenine at position 372 (SEQ ID No.: 90).

Although the antisense compounds of the present invention are shown for convenience as "nucleic acid" in
15 Sequence Listing, the compounds are not necessarily nucleoside derivatives as far as they are capable of hybridizing to the target sequences, as discussed above. Furthermore, part of the sequence (preferably 5 or less bases) may be replaced by any non-complementary bases to
20 such an extent that their hybridization ability are not spoiled.

It may be possible to introduce the antisense compounds of the present invention into cultured cells, for example, by incorporating said antisense compounds as such
25 into the culture medium. The antisense compounds

consisting of about 15-28 bases in the form of phosphorothioate-type or methylphosphonate-type are readily introduced into cells by such a method. In order to effect an active introduction of the antisense compounds, the transfection methods which are commonly applied to animal cells, such as calcium phosphate method, electroporation, or liposome method, may also be used preferably.

When intravenously administered to human subjects, it appears that about half of the antisense compounds administered will be absorbed by liver, judging from the results of experiments in animals. Depending on the structure and property of an antisense compound, the uptake efficiency can be increased by, for example, protecting the antisense compound with liposomes or attaching a substance capable of recognizing cells to the antisense compound.

The process for preparing the antisense compounds of the present invention is described in more detail below.

(1) Preparation of mRNA T7N1-19

For example, plasmid pUCT71-19 (European Patent Publication 518,313) is firstly prepared by the alkaline method and subsequent CsCl density gradient ultracentrifugation. Then, the plasmid is digested completely with EcoRI to obtain a linear DNA which has been cut at a site 3' to the clone T7N1-19. About 80-100 µg of

HCV mRNA T7N1-19 may be obtained from about 1 μ g of this linear DNA by in vitro transcription using T7 RNA polymerase. This reaction may be effected by means of RNA TRANSCRIPTION Kit (Stratagene), although the reagents
5 separately prepared may also be used under the condition in which T7 RNA polymerase is active. The resultant mRNA may be identified by northern hybridization. The probe may be prepared by the labelling method using a DNA fragment of 3'-terminal region of the clone T7N1-19. The amount of
10 mRNA may be calculated from the absorbance at 260 nm.

(2) Synthesis of antisense compounds

Phosphodiester-type oligonucleotides and phosphorothioate-type oligonucleotides may be synthesized by means of, for example, a DNA Synthesizer Model 394
15 (Applied Biosystems). The reaction is carried out under the condition of dimethoxytrityl-ON. The desired antisense compound may be obtained after the purification with HPLC (all of the diastereomers of the desired product are combined) and the subsequent treatment with acetic acid.

20 (3) Measurement of the inhibitory effects of the antisense compounds on the translation of HCV-derived proteins using the in vitro translation method

The in vitro translation is carried out using the mRNA obtained in the above step (1) to express the HCV-
25 derived proteins encoded by the mRNA under the IRES activity. The in vitro translation uses, for example,

Rabbit Reticulocyte Lysate and Canine Microsomal Membranes (Promega). The microsomal membrane is considered to be necessary for the cutting, by signal peptidase, the junctions between the core protein and the envelope (E1) as well as the envelope (E1) and E2 (NS1). [³⁵S]-methionine is incorporated into the translated polypeptide. The polypeptides containing the HCV core protein may be immunoprecipitated with anti-HCV core antibody, electrophoresed on SDS-PAGE, and analyzed on BIO-IMAGE ANALYZER BAS 2000 (Fuji Film).

In order to determine the inhibitory effect on the translation, the antisense compound is preferably mixed with in vitro translation reagents immediately before the mRNA and in vitro translation reagents are mixed. As the result of such studies, it is confirmed that the antisense compounds of the present invention consisting of 10-34 bases (preferably about 15-30 bases) which may be designed on the basis of the HCV gene sequence are closely associated with the inhibitory effects.

(4) Translation inhibition of HCV gene by antisense compounds in cell evaluation system using recombinant vaccinia virus

It is known that a homologous recombination occurs between a particular sequence found in vaccinia virus gene, which is connected with both termini of a

foreign gene, and the corresponding sequence to said particular sequence in the vaccinia virus gene. Taking advantage of this homologous recombination, a recombinant vaccinia virus can be prepared, into which HCV gene has
5 been inserted. The resultant vaccinia virus can be used to infect an appropriate cell, and the HCV gene is allowed to express in the cell. Accordingly, translation inhibitory effect of the antisense compounds of the present invention can be measured by the use of a cell evaluation system
10 which permits assay of expressed HCV protein.

Specifically, HCV-derived gene is inserted into hemagglutinine (HA) gene of vaccinia virus, as described hereinafter in the working example. HA is not essential for the growth of vaccinia virus. However, loss of HA gene
15 function results in vaccinia virus which is deficient in hemagglutination ability, and can be detected by virus plaque stain by chick erythrocyte. Accordingly, said HA gene is conveniently used as an inserting site of a foreign gene. However, said inserting site is not limited to the
20 HA gene as far as the growth of the virus is not adversely affected and the virus containing a foreign gene can easily be detected after the insertion. The HCV-derived gene to be inserted into the vaccinia virus must be a gene which contains IRES region locating at 5' untranslated region.
25 As previously stated, it is said that a polypeptide coded

by the HCV genome is expressed as a single polypeptide (precursor protein) comprising about 3,000 amino acid residues, and the polypeptide results in various functional proteins 24 through processing. The precursor proteins
5 consists of core protein, E1 (envelope) protein, E2 (NS1 or envelope 2) protein, etc. aligned from N-terminus in this order. This means that the HCV genome is composed of untranslated region, core protein-encoding region, E1
10 protein-encoding region, etc. aligned from 5' terminus in this order. In order to determine the magnitude of the translation inhibitory effect of HCV polypeptide, it is essential that HCV-derived polypeptide is normally produced. Accordingly, the HCV-derived gene to be inserted
15 must be a gene which contains at least the IRES region locating at 5' untranslated region and core protein-encoding region locating at 3' side thereof. More specifically, such HCV-derived gene may be a gene comprising the base sequence beginning from the base at position 25-30 in SEQ ID No. 1 and containing subsequent
20 ~910 bp. Since this gene encodes the core protein, the expression of the gene can be measured by detecting a protein of about 22KDa through western blotting.

The HCV-derived gene is inserted into a vector such as pUC19, after linked with a promoter at the 5'
25 terminal. The promoter may be anything as far as it

functions in vaccinia virus. High-expression promoter is preferable, such as an early promoter derived from vaccinia virus. More specifically, it is preferred to use 7.5K promoter from vaccinia virus (cell 125 805-813, 1981) and
5 its variant which contains point mutation (J. Mol. Biol., 210) 749-769, 1988). It is one of preferred embodiments of the present invention to use a combination of a synthetic DNA represented by SEQ ID No. 406 and the above-noted promoter. When a reporter gene of luciferase gene is
10 inserted at 3' side of HCV gene, the fused gene yields a fused protein. Said fused protein consists of HCV-derived polypeptide and a polypeptide encoded by the reporter gene, and therefore, the HCV-derived polypeptide is indirectly measured by measuring the polypeptide encoded by the
15 reporter gene after processing under appropriate conditions. The HCV gene contains a signal sequence at which the core protein and E1 protein undergo processing under an appropriate condition. Accordingly, where translation inhibitory activity of HCV core protein is
20 measured, it is desirable to make design so that the core protein is cut at its C-terminal, taking advantage of the signal sequence. Construction of a vector can be conducted in conventional manners.

A vector DNA is prepared in conventional manner
25 using the transfer vector thus obtained. The DNA and

vaccinia virus are combined so that homologous recombination may occur between them. A cell line derived from human beings is infected with the recombinant vaccinia virus thus obtained. The recombinant protein expressed in the infected cells is recovered according to any one of conventional methods, and the amount of the HCV-derived polypeptide is measured by a known method such as western blotting.

The antisense compound of the present invention is added before and/or after the infection of cells with the recombinant vaccinia virus. The translation inhibitory effect of the antisense compounds of the invention is determined after comparison of the amount of expressed polypeptide with that obtained when the antisense compound is not added, or when there is added other antisense compound which has low homology with a complementary stand of a HCV or reporter gene and therefore hardly forms a hybrid with the HCV gene. Many groups including American bio-venture companies have described about the dose of antisense compounds. According to such information, it has been shown in incurable diseases such as HIV patients that an antisense compound which exhibits its effect on cultured cells (animal cells) at 10-100 μ M also exhibits its effect on human subjects to some extent. Based on those values, we aimed for the antisense compounds

which exhibit their effects in the in vitro translation study at 10 μ M or less, and preferably at 1 μ M or less, so that they may exhibit their effects on cultured cells at 50 μ M or below after taking the contribution of the factors such as permeability and uptake efficiency into consideration.

As a result, the antisense compounds which realize the above aim have been found as described in the following examples. These compounds are expected to exhibit their effects on cultured cells expressing the HCV gene and even on HCV patients.

Brief Description of the Drawings

Fig. 1 is an electrophoretic pattern which shows the translational inhibitory effects of antisense compounds of the present invention, Anti 1, SMS 13, SMS 14, SMS 16, SMS 17, and SMS 18 (the final concentration = 1.18 μ M) as measured in in vitro translation system.

Fig. 2 is an electrophoretic pattern which shows the correlation between the concentration of the antisense compounds of the present invention, SMS 16, SMS 17, and SMS 18, and their translational inhibitory effects.

Fig 3. shows Western Blotting of HCV core protein expressed by recombinant vaccinia virus. Lane 1 represents recombinant vaccinia virus rVV5CL and Lanes 2 and 3 represent wild-type vaccinia virus.

Fig. 4 shows an enzymatic activity of luciferase expressed by WRL 68 cell infected by the recombinant vaccinia virus rVV5CL in the presence of antisense compounds of the present invention at concentrations of 0.25, 0.5, and 2.5 μM . The ordinate indicates an enzymatic activity of luciferase ($\times 10^{-20}$ mol/8 μM). The legend "antisense(-)" means an enzymatic activity of luciferase in the absence of the antisense compounds of the invention.

Fig. 5 shows relative values of the enzymatic activity of the expressed luciferase when an average enzymatic activity of antisense(-) is stipulated as 100.

Fig. 6 shows an enzymatic activity of luciferase expressed by WRL68 cell infected by the recombinant vaccinia virus rVV5CL in the presence of antisense compounds of the present invention at concentrations of 0.25, 0.5, and 1.5 μM . The activity is a relative value to the antisense(-).

The following examples further illustrate the present invention. The examples are illustrative only and are not intended to limit the scope of the invention in any way.

Example 1: Preparation of mRNA T7N1-19

A hundred μg of plasmid pUCT7119 (European Patent Publication 518,313) which contains the clone T7N1-19 shown as SEQ ID NO: 1 in the cloning sites of pUC19 was prepared

by the alkaline method and the subsequent density gradient ultracentrifugation using CsCl (Molecular Cloning: A Laboratory Manual, 2nd ed., 1.33-1.52, 1989).

5 Ten µg of this highly purified plasmid was digested completely with EcoRI to obtain a linear DNA which had been cut at a site 3' to the clone T7N1-19. One µg of the linear DNA was subjected to a reaction in 50 µl of a reaction mixture consisting of 40 mM Tris-HCl (pH 8.0), 5 mM DTT, 50 µg/ml BSA, 2 mM each NTP, 40 mM MgCl₂, 1 mM spermidine, 50 units of RNase inhibitor, and 1.42 µg of T7 RNA polymerase. After 20 min at 37 °C, 10 unit of T7 RNA polymerase was added and the mixture was further incubated for 20 min at 37 °C. Finally, 10 units (1 µl) of DNase I (Stratagene) was added, and the mixture was incubated for 15 10 min at 30 °C. The reaction was then terminated by adding 50 µl of phenol/chloroform (1/1) mixture. After mixing, 50 µl of the aqueous phase was recovered. In order to precipitate RNA, the aqueous phase was mixed with 5.5 µl of 3M sodium acetate (pH5.5) and then with 150 µl of ethanol. The mixture was then centrifuged at 15,000 rpm for 15 min, and the resultant RNA (transcript) was dried.

20 The RNA thus obtained was dissolved in 30 µl of DEPC-treated sterile water (Molecular Cloning: A Laboratory Manual, 2nd ed., 7.26, 1989). Three µl aliquot of the resultant solution was used to measure the absorbance at 25

260 nm, and the amount of RNA was calculated from the absorbance on the assumption that 1 OD = 40 µg/ml. The amount of RNA thus calculated was about 80 µg. In order to examine the length of the transcript, an agarose electrophoresis using formamide was carried out (Molecular Cloning: A Laboratory Manual, 2nd ed., 7.43, 1989). On the gel, the RNA was shown as a single band, and its length was proper as compared with the molecular markers (GIBCO BRL: 0.24-9.5 Kb RNA Ladder). Furthermore, the band on the agarose gel was transferred onto a membrane, and northern hybridization (Molecular Cloning: A Laboratory Manual, 2nd ed., 7.39-7.52, 1989) was carried out to confirm that the transcribed RNA was surely derived from the clone T7N1-19. The probe used in this hybridization was prepared according to the labelling method (Molecular Cloning: A Laboratory Manual, 2nd ed., 10.13-10.17, 1989) from a DNA fragment which has a sequence of the clone N19 at the 3'-region of the clone T7N1-19 .

Example 2: In vitro synthesis of HCV-derived proteins and analysis thereof

The mRNA T7N1-19 synthesized in Example 1 has almost the same structure as 2,007 bases of the 5'-region of the HCV genome gene (European Patent Publication 518,313) which is a single stand RNA. The difference between the above two RNAs resides in that the promoter

enhancing sequence of T7 which acts on T7 RNA polymerase has been attached to the 5'-terminal of the HCV gene in the former RNA. The in vitro translation was initiated by adding a mixture consisting of 11.375 μ l of Rabbit

5 Reticulocyte Lysate (Promega), 1.17 μ l of Canine Microsomal Membranes (Promega), 5.2 μ l of Amino Acid Mixture (Promega), 1.3 μ l (729 KBq) of L-[³⁵S]-methionine (Amersham), and 0.2 μ l of RNase Inhibitor (Takara Shuzo) to about 3.5 μ g of the transcript obtained above so as to

10 obtain the final volume of 14.37 μ l. The reaction was accomplished substantially according to the protocol described in "Translation in vitro Technical Manual" (Promega). Similar reaction was carried out without the

RNA (transcript) in order to check the reagents used,

15 whereby nothing was synthesized. In the control, 0.5 μ g of E. coli β -lactamase mRNA (supplied by Promega along with Canine Microsomal Membranes) was substituted for about 3.5 μ g of the transcript.

After incubating for 1 hour and 15 min at 30 °C,

20 only polypeptides including the HCV core protein were separated by the immunoprecipitate method, and then subjected to SDS-PAGE. This is because it was expected that the amount of proteins per lane may become too plenty to analyze synthesized proteins, if the whole reaction

25 mixture is used for the electrophoresis.

Thus, 2.5% SDS was added to the whole translation reaction mixture so that the final concentration of SDS became 0.5%. Four volume of RIPA buffer 1 (1% Triton X-100, 1% sodium deoxycholate, 0.15 M NaCl and 50 mM Tris-HCl (pH7.5)) was then added, and the mixture was cooled on ice. One μ l of anti-HCV core antibody (purified from rabbit serum, polyclonal antibody, 1 μ g/1 μ g) was then added and the resultant mixture was allowed to stand for 1 hour at 0 °C. The mixture was then mixed with 3.125 μ l of zysorbin (Zymet, 10% w/v), and allowed to stand for 1 hour at 0 °C. Then, the mixture was centrifuged at 3000 rpm for 3 min. The precipitate was washed by adding 100 μ l of RIPA buffer 2 (1% Triton X-100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl and 50 mM Tris-HCl (pH7.5)), and the same procedure was repeated with 100 μ l of RIPA buffer 3 (1% Triton X-100, 1% sodium deoxycholate, 0.1% SDS, 0.15 M NaCl, 50 mM Tris-HCl (pH7.5) and 1 mg/ml BSA). After the final washing with RIPA buffer 2, the resultant precipitate was suspended in 8 μ l of SDS loading buffer (9.1% Tris-HCl (pH6.8), 16.1% (v/v) glycerine, 4.2 M urea, 3.15% SDS, 12.7% (v/v) β -mercaptoethanol and 0.04% BPB).

This sample was then boiled at 95 °C for 5 min. Eight μ l of the sample thus obtained was applied to 0.1% SDS-15.0% polyacrylamide gel (70 x 85 x 1 mm). In this electrophoresis, Rainbow [14 C] methylated protein molecular

weight markers (Amersham, molecular weight range: 14,300-
200,000) was used as marker proteins. The electrode buffer
utilized was a Tris buffer (25 mM Tris (pH8.3), 192 mM
glycine and 0.1% SDS). The electrophoresis was carried out
5 with a constant electric current of 30 mA for 45 min. The
gel was then placed on a Whatman 3MM filter, covered with a
transparent wrapping film (Saran wrap), and dried with a
gel drier. The dried gel was held between imaging plates
(Fuji Film, Type BAS-III) and put into a designated
10 cassette, and allowed to stand at room temperature for 12
hours (these procedures were done according to the protocol
for BIO-IMAGE ANALYZER BAS 2000 of Fuji Film). By
analyzing the imaging plate on BIO-IMAGE ANALYZER, about 22
KDa HCV-derived core protein and its about 61 KDa precursor
15 (polypeptide consisting of 555 amino acids) labelled with
³⁵S-methionine were detected as sharp bands.

Example 3: Synthesis of antisense compounds

From the region beginning from thymine at
position 27 and ending at cytosine at position 410, a lot
20 of specific sequences consisting of about 10-34 bases to
which antisense compounds are to be hybridized were set up,
and the complementary sequences determined by such
specified base sequences were used as the sequences of
antisense oligonucleotides. The antisense oligonucleotides
25 were synthesized using Applied Biosystems DNA Synthesizer

Model 394. The reaction was carried out under the condition of dimethoxytrityl-ON, and the protective groups on the bases which were added during the synthesis were removed according to the protocol provided by the manufacturer. The synthesized oligonucleotides were purified by HPLC. Although, in the case of phosphorothioate-type oligonucleotides, they are not separated in a single peak as in the case of phosphodiester-type oligonucleotides, all of the diastereomers were combined into one lot. The protective group on the hydroxy group at the 5'-terminal (dimethoxytrityl group) was deprotected with acetic acid aqueous solution according to the conventional method to obtain a desired antisense compound. Such antisense compounds were further treated with phenol and quantified from the absorbance at 260 nm on the assumption that 1 OD = 35 µg/ml. The sequences of the antisense compounds thus synthesized are shown below.

Name	Length (mer)	Sequence (5'-terminal to 3'-terminal)
Anti 1	30	CCGCAGACCACTATGGCTCTCCCGGGTGGG (adenine at position 27 in SEQ ID NO: 38 was replaced by thymine)
Anti 2	30	TCATGATGCACGGTCTACGAGACCTCCCGG (SEQ ID NO: 64)
Anti 3	15	GTGCTCATGATGCAC (SEQ ID NO: 105)

2104649

- 31 -

	Anti 4	15	ACCACAAGGCCTTTC (SEQ ID NO: 50)
	Anti 5	30	TCATGATGCACGGTCTACGAGACCTCpCpCpGpG (SEQ ID NO: 64)
5	Anti 6	30	TCATGATGCACGGTCTACGAGACCpTpCpCpCpGpG (SEQ ID NO: 64)
	Anti 7	20	AGTACCACAAGGCCTTpTpCpGpC (SEQ ID NO: 58)
10	Anti 8	20	AGTACCACAAGGCCpTpTpTpCpGpC (SEQ ID NO: 58)
	SMS 1	19	GTGCTCATGATGCACpGpGpTpC (SEQ ID NO: 102)
	SMS 2	30	CCGCAGACCACTATGGCTCTCCCGGGpApGpGpG (SEQ ID NO: 38)
15	SMS 3	19	CCGGGAGGGGGGGTCTCpTpGpG (SEQ ID NO: 106)
	SMS 4	26	TACTCACCGGTTCCGCAGACCpCpTpApT (SEQ ID NO: 107)
20	SMS 9	20GTAG	TTCCTCACAGGGGAGT (SEQ ID NO: 109)
	SMS 10	20	TCATACTAACGCCATGGCTA (SEQ ID NO: 108)
25	SMS 11	20	GGGGTCCTGGAGGCTGCACG (SEQ ID NO: 6)
	SMS 13	20	CTATGGCTCTCCCGGGAGGG (SEQ ID NO: 35)
	SMS 14	20	CCGCAGACCACTATGGCTCT (SEQ ID NO: 41)
30	SMS 15	20	ACCACTATGGCTCTCCCGGG (SEQ ID NO: 110)
	SMS 16	20	GCTCATGATGCACGGTCTAC (SEQ ID NO: 98)
35	SMS 17	20	TCATGATGCACGGTCTACGA (SEQ ID NO: 90)

2104649

- 32 -

	SMS 18	20	TCCTGGAGGCTGCACGACAC (SEQ ID NO: 22)
	SMS 19	20	ATGATGCACGGTCTACGAGA (SEQ ID NO: 83)
5	SMS 20	15	GCTCATGATGCACGG (SEQ ID NO: 103)
	SMS 21	20	GGTTCCGCAGACCACTATGG (SEQ ID NO: 111)
10	SMS 22	20	TGGAGGCTGCACGACACTCA (SEQ ID NO: 112)
	SMS 23	20	GGTCCTGGAGGCTGCACGAC (SEQ ID NO: 14)
	SMS 24	20	CAGTACCACAAGGCCTTTCG (SEQ ID NO: 113)

15 In the above sequences, the letter "p" inserted between two bases indicates that the phosphodiester linkage at that position is not phosphorothioate-type but is an unmodified phosphodiester linkage. The phosphate linkages between the other bases are all phosphorothioate-type.

20 **Example 4:** Inhibitory effects of antisense compounds on the synthesis of HCV-derived proteins

The experiments were carried out as described below using antisense compounds synthesized in Example 3.

25 The in vitro translation was accomplished as described in Example 2 by adding a lysate mixture consisting of 11.375 µl of Rabbit Reticulocyte Lysate (Promega), 1.17 µl of Canine Microsomal Membranes (Promega), 5.2 µl of Amino Acid Mixture (Promega), 1.3 µl

(729 KBq) of L-[³⁵S]-methionine (Amersham), and 0.2 µl of RNase Inhibitor (Takara Shuzo) into an Eppendorf tube containing mRNA T7N1-19 so as to obtain the final volume of 14.37 µl. The Eppendorf tube contained also an antisense compound on its wall so that the lysate mixture was mixed with the antisense compound prior to the mixing with mRNA. All of the procedures after the reaction were carried out as described in Example 2.

In these experiments, at least three in vitro translation reactions per experiment were carried out in the absence of an antisense compound and those three reactions were arranged on an electrophoresis gel disconnectedly. Furthermore, each of the reagents used in one experiment such as Rabbit Reticulocyte Lysate, Amino Acid Mixture, Canine Microsomal Membranes, and L-[³⁵S]-methionine was taken from the same lot, and combined together to make a mixture which was then divided into aliquots.

The inhibitory effects of antisense compounds on the translation of the HCV core protein were analyzed on BIO-IMAGE ANALYZER BAS 2000 (Fuji Film), and the results were printed out by Pictrography (Figures 1 and 2).

Among the numerous antisense compounds designed in the present invention, those particularly effective are antisense compounds which are directed to the regions

positioned at 131-146, 151-156, 175-180, 285-289, 309-314, 355-359, or 369-373 in SEQ ID NO: 1.

These antisense compounds were examined in the in vitro translation system at a final concentration of, for example, about 0.12 μM , about 0.6 μM , about 1.2 μM , about 2.9 μM , or about 5.8 μM . In the experiment carried out with a concentration of about 1.2 μM , the amount of the produced HCV core protein has decreased, in comparison with the case without the antisense compound, to about 1/5 to about 1/10 or less for Anti 1, SMS 1, SMS 11, SMS 13 and SMS 14, and to about 1/10 to about 1/40 or less for SMS 16, SMS 17, and SMS 18 (Figures 1 and 2). Antisense compounds, Anti 1, Anti 4, Anti 7, SMS 1, SMS 2, SMS 11, SMS 13, SMS 14, SMS 16, SMS 17, and SMS 18 at a final concentration of from about 2.9 μM to about 5.8 μM did not affect the translation of E. coli β -lactamase mRNA. In the reaction carried out in the presence of SMS 9 (an antisense compound directed to the sequence consisting of 20 bases from adenine at position 66 to cytosine at position 85: SEQ ID NO: 109) which was evaluated for the purpose of comparison, the amount of the produced HCV core protein has decreased only slightly. Although the amount of the produced HCV core protein was decreased by SMS 3, this antisense compound has affected also the translation of E. coli β -lactamase mRNA to some extent.

Thus, it was confirmed that the antisense compounds of the present invention act specifically on the mRNA of HCV to inhibit the translation of HCV gene without adversely affecting the translation system as such.

Example 5: Construction of a recombinant vaccinia virus rVV5CL

(1) Preparation of a transfer vector for constructing a recombinant vaccinia virus

5 The HA protein gene was purified from vaccinia virus strain WR according to the procedure described in Example 1 of Japanese Patent Publication (kokai) 63-63380. Vaccinia virus strain WR was purified and suspended in 50mM Tris-HCl (pH 7.4) containing 1mM EDTA and 0.5% sodium
10 dodecylsulfate. To this suspension was added proteinase K at 250-1000 µg/ml. The resultant mixture was incubated overnight at 37 °C, and then extracted thrice with buffer-saturated phenol-chloroform (1:1). Then, viral DNA was
15 precipitated with ethanol. (Hereinafter, the term "ethanol precipitation" refers to a procedure in which an aqueous phase is mixed with one tenth volume of 3M sodium acetate or equal volume of 4M ammonium acetate and 2.5 fold volume of ethanol, then subjected to centrifugation using a rotor having about 5 cm of radius at 15,000 rpm for 15min at 4
20 °C, and the resultant precipitate is dried.) The DNA thus obtained was dissolved in 10 mM Tris-HCl (pH 8.0)

containing 1mM EDTA, digested with HindIII, and subjected to agarose gel electrophoresis to isolate an about 50 kb HindIII A fragment. This HindIII A fragment was digested with SalI in high-salt buffer (50mM Tris-HCl, 100mM NaCl, 10mM MgCl₂, 1mM DTT (pH 7.5)), and then subjected to agarose electrophoresis to isolate an about 1.8kb HindIII-SalI fragment which is present at 3' terminal of the HindIII A fragment. This DNA fragment was blunt-ended with T4 DNA polymerase. By means of DNA Ligation Kit (Takara Shuzo), this DNA fragment was incorporated into pUC 19 cloning vector which had been digested with HindIII and EcoRI, and then blunt-ended with T4 DNA polymerase.

A 7.5k protein promotor fragment was also purified from vaccinia virus strain WR according to the procedure described in Example 4 of Japanese Patent Publication (kokai) 63-63380. Viral DNA prepared as described above was digested with SalI in high-salt buffer, and subjected to agarose electrophoresis to obtain an about 0.9kb SalI fragment. Separately, plasmid pUC 18 was digested with SalI in high-salt buffer, and subjected to extraction with phenol and ethanol precipitation to obtain a linear plasmid. This linear plasmid was then ligated to the about 0.9kb SalI fragment described above in ligation buffer (66mM Tris-HCl, 1mM ATP, 5mM MgCl₂, 5mM DTT (pH 7.6)) by means of T4 DNA ligase. The ligation mixture was

used to transform E. coli strain JM103. Plasmid p0901 was obtained by screening in which each of the plasmids from transformed clones was digested with SalI to obtain the above DNA fragment which was then digested with RsaI, AluI,
5 HapII and DdeI for analysis. This plasmid was digested with RsaI and HincII in medium-salt buffer (10mM Tris-HCl, 50mM NaCl, 10mM MgCl₂, 1mM DTT (pH 7.5)), and then subjected to agarose electrophoresis to isolate a 0.26kb blunt-ended RsaI-HincII fragment. This fragment includes
10 7.5k protein promotor. This DNA fragment was incorporated by means of DNA Ligation Kit (Takara Shuzo) into pUC 19 cloning vector which had been digested with HincII.

In the ligation reaction described above, 5-10 ng of vector DNA which had been prepared as described below
15 was used. The pUC 19 cloning vector was cut with restriction enzymes HindIII and EcoRI or HincII (Toyobo), treated with phenol/chloroform, and subjected to ethanol precipitation. The resultant linear DNA was dephosphorylated at its 5' end using alkaline phosphatase
20 (Boehringer-Mannheim) (Molecular Cloning: A Laboratory Manual, 1982, Cold Spring Harbor Laboratory Press), treated with phenol/chloroform, and then subjected to ethanol precipitation.

DNA thus constructed was used to transform E. coli JM109 using competent cells (COMPETENT HIGH) supplied
25

by Toyobo according to the manufacturer's instruction.

From transformants thus obtained, a plasmid in which the 5' side of the HA protein gene is present at the same side as the EcoRI site in the multicloning site of pUC was selected by conventional miniscreening (Molecular Cloning: A Laboratory Manual, 1982, Cold Spring Harbor Laboratory Press), and designated as pUCHA. In addition, a plasmid in which the 5' side of the 7.5k promotor is present at the same side as the HindIII site in the multicloning site of pUC 19 was also selected and designated as pUC7.5.

Plasmid DNAs of pUCHA and pUC7.5 were prepared from corresponding transformants and sequenced by means of a fluorescence sequencer GENESIS 2000 system (DuPont). Synthetic sequence primers used in this sequencing were 5'd(GTAAAACGACGGCCAGT)3' (SEQ ID NO: 399) and 5'd(CAGGAAACAGCTATGAC)3' (SEQ ID NO: 400).

One µg of plasmid pUC7.5 was cut with a restriction enzyme SmaI, treated with phenol/chloroform, subjected to ethanol precipitation, dephosphorylated at its 5' end using alkaline phosphatase (Boehringer-Mannheim) (Molecular Cloning: A Laboratory Manual, 1982, Cold Spring Harbor Laboratory Press), treated with phenol/chloroform, and subjected to ethanol precipitation. Into 10 ng of DNA thus obtained, 5 ng of synthetic linker

5'd(PCAGATCTGCAAGCTTG)3' (SEQ ID NO: 401) was inserted by means of DNA Ligation Kit (Takara Shuzo). The DNA thus constructed was used to transform E. coli DH5 using competent cells (COMPETENT HIGH) supplied by Toyobo according to the manufacturer's instruction. From transformants thus obtained, plasmid pUC7.5GH in which the above synthetic linker has been incorporated so that BglII and HindIII sites align in this order in the same direction as the 7.5k promoter was obtained by conventional miniscreening.

In order to modify the 7.5k promoter, this plasmid was used to amplify a DNA fragment having a specific sequence by PCR method according to the method of Saiki et al. [Nature, 324, 126, (1986)].

To a mixture of 10 ng of plasmid pUC7.5GH, 10 µl of 10xPCR buffer (100mM Tris-HCl, pH 8.3, 500mM KCl, 15mM MgCl₂, 1% gelatin), 16 µl of 1.25mM 4dNTP, and each 5 µl (20 µM) of synthetic DNA primers 5'd(CAGGAAACAGCTATGAC)3' (SEQ ID NO: 402) and 5'd(GAATAGTTTTTCAATTTTACG)3' (SEQ ID NO: 403), or each 5 µl (20 µM) of synthetic primers 5'd(CGTAATAATTGAAAACTATTC)3' (SEQ ID NO: 404) and 5'd(GTAAAACGACGGCCAGT)3' (SEQ ID NO: 405) was added water so as to obtain the final volume of 100 µl. The mixture was firstly heated at 95 °C for 5 min and then cooled rapidly to 0 °C. After 1min, 0.5 µl of Taq DNA polymerase

(7 unit/ μ l, AmpliTaqTM, Takara Shuzo) was added and the mixture was covered with mineral oil. This sample was subjected to 30 cycles of 1 min at 95 °C, 1 min at 48 °C, and 1 min at 72 °C on DNA Thermal Cycler (Perkin-Elmer Cetus Instruments). At the end of this period, the reaction mixture was maintained at 72 °C for 7 min, and then treated with phenol/chloroform. After ethanol precipitation, two amplified DNA fragments which are 250 bp and 110 bp in length were obtained. These fragments were purified on 5% acrylamide gel. To a mixture of each 5 ng of DNA fragments obtained above, 10 μ l of 10xPCR buffer (100mM Tris-HCl, pH 8.3, 500mM KCl, 15mM MgCl₂, 1% gelatin), 16 μ l of 1.25mM 4dNTP, and each 5 μ l (20 μ M) of synthetic DNAs 5'd(CAGGAAACAGCTATGAC)3' (SEQ ID NO: 402) and 5'd(GTAAAACGACGGCCAGT)3' (SEQ ID NO: 405) was added water so as to obtain the final volume of 100 μ l. The mixture was firstly heated at 95 °C for 5 min and then cooled rapidly to 0 °C. After 1 min, 0.5 μ l of Taq DNA polymerase (7 unit/ μ l, AmpliTaqTM, Takara Shuzo) was added, and the mixture was covered with mineral oil. This sample was subjected to 30 cycles of 1 min at 95 °C, 1 min at 48 °C, and 1 min at 72 °C on DNA Thermal Cycler (Perkin-Elmer Cetus Instruments). At the end of this period, the reaction mixture was maintained at 72 °C for 7 min, and then treated with phenol/chloroform. After ethanol

precipitation, an amplified DNA fragment which is 330bp in length was obtained. This amplified fragment was digested with restriction enzymes EcoRI and PstI, and purified on 5% acrylamide gel. Five ng of the DNA fragment thus obtained
5 was incorporated by means of DNA Ligation Kit (Takara Shuzo) into pUC 19 which had been digested with EcoRI and PstI. The resultant vector was used to transform E. coli DH5 using competent cells (COMPETENT HIGH) supplied by Toyobo according to the manufacturer's instruction. From
10 transformants thus obtained, plasmid pUCSP which has a potent promotor of vaccinia virus was isolated by conventional miniscreening (Molecular Cloning: A Laboratory Manual, 1982, Cold Spring Harbor Laboratory Press). The DNA fragment inserted into the multicloning site of the
15 above plasmid was sequenced using a fluorescence sequencer GENESIS 2000 system (DuPont).

A synthetic DNA (SEQ ID NO: 406) which was designed to have BamHI and BglII sites at the ends of the promotor described in the 40th General Meeting of Japan
20 Virology Society Abstract 4075,
5'd(GATCCAAAAATTGAAAACTAGTCTAATTATTGCACGGA)3'
3'(GTTTTTAACTTTTTGATCAGATTAAATAACGTGCCTCTAG)5'
was inserted into BamHI and BglII sites of plasmid pUCSP by conventional method using DNA Ligation Kit (Takara Shuzo)
25 according to the manufacturer's instruction. The resultant plasmids were used to transform E. coli DH5. A plasmid

pUCSE in which six synthetic DNAs had been inserted tandem in correct direction was then isolated by miniscreening.

5 The plasmid pUCSE thus obtained was digested with restriction enzymes PstI and EcoRI. The reaction mixture was treated with phenol/chloroform and subjected to ethanol precipitation. The precipitated DNA was blunt-ended with T4 DNA polymerase, and then purified on 5% acrylamide gel to obtain a 550bp DNA fragment. Five ng of the DNA fragment thus obtained was ligated to 10 ng of plasmid 10 PUCHA which had been digested with NruI. The resultant plasmids were used to transform E. coli DH5 using competent cells (COMPETENT HIGH) supplied by Toyobo according to the manufacturer's instruction. From the transformants thus obtained, plasmid pHASE in which the vaccinia viral 15 promotor had been inserted in the same direction as the HA gene was isolated by conventional miniscreening (Molecular Cloning: A Laboratory Manual, 1982, Cold Spring Harbor Laboratory Press). The DNA fragment which had been inserted in the multicloning site of the above plasmid was 20 sequenced by means of a fluorescence sequencer GENESIS 2000 system (DuPont). DNA sequence thus determined which begins from the SalI site and ends at the HindIII site of the multicloning site of that plasmid is shown as SEQ ID NO: 409 in Sequence Listing.

The segment of the HCV gene beginning from its 5' end and ending at the core protein gene was amplified by PCR method. To a mixture of five ng of DNA of clone T7N119 described in Example 28 [2] of European Patent Publication

5 518,313, 10 μ l of 10x PCR buffer (100mM Tris-HCl, pH 8.3, 500mM KCl, 15mM MgCl₂, 1% gelatin), 16 μ l of 1.25mM 4dNTP, and each 5 μ l (20 μ M) of synthetic DNAs

5'd(CGAAGCTTGCCAGCCCCCTGATGGG)3' (SEQ ID NO:407) and 5'd(CCGGATCCCGAAGCTGGGATGGTCAAC)3' (SEQ ID NO:408) was

10 added water so as to obtain the final volume of 100 μ l, and the mixture was firstly heated to 95 °C for 5 min, and then cooled rapidly to 0 °C. After 1 min, 0.5 μ l of Taq DNA polymerase (7 unit/ μ l, AmpliTaqTM, Takara Shuzo) was added, and the mixture was covered with mineral oil. This sample

15 was subjected to 30 cycles of 1 min at 95 °C, 1 min at 58 °C, and 1 min at 72 °C on DNA Thermal Cycler (Perkin-Elmer Cetus Instruments). At the end of this period, the reaction mixture was maintained at 72 °C for 7 min, and then treated with phenol/chloroform. After ethanol

20 precipitation, an amplified DNA fragment which is 910bp in length was obtained. This amplified DNA fragment was digested with restriction enzymes HindIII and BamHI, and then purified on 5% acrylamide gel. The purified DNA fragment was inserted into HindIII and BamHI sites of

25 PicaGeneTM cassette vector (Toyo Ink) for luciferase assay.

Plasmid pCS5CL in which the segment of the HCV gene beginning from its 5' end and ending at the core protein gene had been inserted upstream of the luciferase gene in the same direction was obtained by miniscreening.

5 Plasmid pCS5CL was partially digested with EcoRI, and then completely digested with HindIII. The reaction mixture was subjected to agarose electrophoresis to isolate a 2.6 kbp fragment. This fragment was inserted into HindIII and EcoRI sites of plasmid pHASE. Then, plasmid
10 pHA5CL which contains, in the vaccinia viral HA protein gene, the vaccinia viral promotor, the segment of the HCV gene beginning from its 5' end and ending at the core protein gene, and the luciferase gene in this order was obtained by miniscreening.

15 (2) Construction of recombinant vaccinia virus rVV5CL

African green monkey kidney-derived cell line CV-1 (Rikagaku Kenkyusho Saibou Kaihatu Ginko RCB0160) which had been cultivated to semi-confluent in a 3.5 cm petri dish was infected with vaccinia virus strain LC16mO
20 (Rinsho-to-uirus, 3(3), 229-235, 1975) at MOI (multiplicity of infection) = 0.1 PFU/cell for 1 hour at room temperature. Separately, plasmid pHA5CL constructed in (1) was isolated and purified from the recombinant E. coli according to the method of Maniatis et al. [Molecular
25 Cloning: A Laboratory Manual, Cold Spring Harbor

Laboratory, 86-96(1982)] to obtain a large amount of the transfer vector pHA5CL DNA. Ten μg of pHA5CL DNA thus obtained was mixed with 30 μl of Lipofectin (Life Technology) in 170 μl of Opti-MEM medium (Life Technology),
5 allowed to stand for 10 min, and used as a transfection solution.

Then, the viral solution was removed from the petri dish, and the cells were washed twice with Opti-MEM medium. The aforementioned transfection solution was mixed
10 with 800 μl of Opti-MEM, and then added to the washed cells. The cells were cultivated in a 5% CO_2 incubator at 37 $^{\circ}\text{C}$. After 4 hours, the medium was removed, and MEM medium containing 10% fetal bovine serum was added to the petri dish. After incubating in a 5% CO_2 incubator at 37
15 $^{\circ}\text{C}$ for 2 days, these infected cells were subjected thrice to freeze-thawing to harvest the virus.

The harvested virus solution contained about 10^6 virus per ml and about 0.1% of which was the recombinant virus. Plaque isolation method described below was used
20 for isolating the recombinant virus. The virus solution was diluted 10^5 times. Separately, rabbit kidney-derived cell line RK-13 (Rikagaku Kenkyusho Saibou Kaihatu Ginko RCB0183) was plated at 2×10^5 cells per 10 cm petri dish, and cultivated. After the medium was removed completely, 1

ml of the above virus solution diluted 10^5 times was added to each petri dish. In order to prevent the drying of the cells, the petri dish was slanted at every 15 min so that the surface was covered with the virus solution. After the
5 cells were thus infected with the virus for 1 hour, MEM medium containing 2% fetal bovine serum was added to each petri dish, and the cells were cultivated in a 5% CO₂ incubator at 37 °C.

After two days, the medium was aspirated to
10 remove the virus solution completely. Three ml of 1% domestic fowl erythrocyte solution was then added slowly to each petri dish, allowed to adsorb for 1 hour at room temperature, and then aspirated completely. The plaques which did not adsorb the domestic fowl erythrocyte were
15 aspirated with pipette, and suspended in 1 ml of PBS by pipetting. This procedure (comprising infection, cultivation for 2 days, and isolation of recombinant virus) is referred herein as the plaque purification procedure. Two µl of the above virus suspension was subjected to the
20 same plaque purification procedure. This procedure was repeated thrice to obtain a recombinant virus rVV5CL containing the HCV-derived gene and the luciferase gene which is free of contamination from a wild strain.
(3) Expression of the hepatitis virus C gene and the
25 luciferase gene by the recombinant vaccinia virus rVV5CL

Human liver-derived cell line WRL68 (fetal human liver cell, ATCC CL68) which had been cultivated on a 24-well plate to about 60% confluent in TS-2 medium containing 10% fetal bovine serum was infected at MOI = 4 PFU/cell for 1 hour at room temperature with the recombinant vaccinia virus rVV5CL which was mixed homogeneously with PBS containing 2% fetal bovine serum. At the end of this period, the cells were washed twice with 500 μ l of Opti-MEM medium, and then cultivated in 500 μ l of Opti-MEM medium in a 5% CO₂ incubator at 37 °C for 16 hours. The medium was then removed, and the infected cells were lysed by adding 100 μ l of SDS loading buffer described above. Twenty μ l of the lysate was boiled, and then subjected to electrophoresis on 12.5% SDS-PAGE according to the conventional technique. Western blotting onto a nitrocellulose filter was then carried out according to the conventional technique. Color development was accomplished by using anti-HCV core antibody in the similar manner to that described in European Patent Publication 518,313. The result is shown in Fig. 3. As can be seen from the figure, the about 22KDa HCV core protein was detected as a major band, indicating that the fusion protein between the HCV core protein and the luciferase protein was expressed in the infected cells and processed by intracellular signal peptidase which recognizes the signal sequence present at

the C terminal of the HCV core protein. The protein bands larger than 22 KDa are considered to be derived from said fusion protein which were not processed sufficiently, because a control run using non-recombinant wild type vaccinia virus didn't show such bands. Thus, the bands detected herein are believed to be derived from a fusion protein between the HCV core protein and the luciferase protein which was expressed in the cells by the recombinant vaccinia virus rVV5CL.

Furthermore, the cell lysate and the color development solution which are supplied along with PicaGeneTM kit (Toyo Ink) were used in order to detect the expression of the luciferase protein in the infected cells. To infected cells cultivated as described above was added 500 µl of said cell lysate solution instead of the SDS loading buffer, and the mixture was allowed to stand for 30 min at room temperature. Five µl of the above mixture was then added to 80 µl of said color development solution, and 10 seconds after, the mixture was measured on MULTI-BIOLUMAT LB9505C (Berthold Japan). As a result, the protein more than about 10^5 per 5 µl of the cell lysate was expressed as compared to that with uninfected cells (background).

Example 6: Inhibitory effect on intracellular translation of the HCV gene by antisense compounds

(1) Synthesis of antisense compounds

Antisense DNAs prepared as described below were used in this experiment.

5 From the region beginning from thymine at position 27 and ending at adenine at position 859, a lot of specific sequences consisting of about 15-30 bases to which antisense compounds are to be hybridized were set up, and the complementary sequences determined by such specified base sequences were used as the sequences of antisense
10 oligonucleotides. The antisense oligonucleotides were synthesized in phosphorothioate type using Applied Biosystems DNA Synthesizer Model 394. The protective groups on the bases which were added during the synthesis were removed according to the protocol provided by the
15 manufacturer. The synthesized oligonucleotides of intended length were purified by HPLC. Although they are not separated in a single peak as in the case of phosphodiester-type oligonucleotides, all of the phosphorothioate type diastereomers of intended length were
20 combined into one lot. The protective group on the hydroxy group at the 5'-terminal (dimethoxytrityl group) was then deprotected with acetic acid aqueous solution according to the conventional method to obtain a desired antisense compound.

2104649

- 50 -

Such antisense compounds were dissolved in sterile water which was prepared by subjecting ultrapure water (Milli-XQ, Millipore, water of about 18.3MΩ·cm) to autoclave. The concentration was quantified from
 5 absorbance at 260 nm using the nearest-neighbor method (Methods in Enzymology, 1989, Academic Press, Vol.180, 304-325). The solutions of antisense compounds were further sterilized with UFC3 OGVOS (Millipore).

The sequences of the antisense compounds thus
 10 synthesized are shown below.

Name	Length (mer)	Sequence (5'-terminal to 3'-terminal)
Anti 1	30	CCGCAGACCACTATGGCTCTCCCGGGTGGG (SEQ ID NO: 38 in which A at position 27 was replaced by T)
Anti 2	30	TCATGATGCACGGTCTACGAGACCTCCCGG (SEQ ID NO: 64)
Anti 4	15	ACCACAAGGCCTTC (SEQ ID NO: 50)
SMS 1	19	GTGCTCATGATGCACGGTC (SEQ ID NO: 102)
SMS 3	19	CCGGGAGGGGGGGTCTCTGG (SEQ ID NO: 106)
SMS 11	20	GGGGTCCTGGAGGCTGCACG (SEQ ID NO: 6)
SMS 13	20	CTATGGCTCTCCCGGGAGGG (SEQ ID NO: 35)
SMS 14	20	CCGCAGACCACTATGGCTCT (SEQ ID NO: 41)

2104649

- 51 -

	SMS 15	20	ACCACTATGGCTCTCCCGGG (SEQ ID NO: 110)
	SMS 16	20	GCTCATGATGCACGGTCTAC (SEQ ID NO: 98)
5	SMS 17	20	TCATGATGCACGGTCTACGA (SEQ ID NO: 90)
	SMS 18	20	TCCTGGAGGCTGCACGACAC (SEQ ID NO: 22)
10	SMS 21	20	GGTTCCGCAGACCACTATGG (SEQ ID NO: 111)
	SMS 22	20	TGGAGGCTGCACGACACTCA (SEQ ID NO: 112)
	SMS 24	20	CAGTACCACAAGGCCTTTTCG (SEQ ID NO: 113)
15	SMS 30	24	CCGCAGACCACTATGGCTCTCCCG (SEQ ID NO: 42)
	SMS 35	20	GGCTCTCCCGGGAGGGGGGG (SEQ ID NO: 360)
20	SMS 36	20	CTCCCGGGAGGGGGGGTCCT (SEQ ID NO: 296)
	SMS 37	20	CGGGAGGGGGGGTCCTGGAG (SEQ ID NO: 233)
25	SMS 43	19	AAGGTTGGGGGGGAAACGG (SEQ ID NO: 392; This compound corresponds to SMS 3 in which bases other than G had been substituted at random.)
	SMS 44	20	GGGAGGGGGGGTCCTGGAGG (SEQ ID NO: 217)
30	SMS 45	20	GAGGGGGGGTCCTGGAGGCT (SEQ ID NO: 188)
	SMS 46	20	GGGGGGGGTCCTGGAGGCTGC (SEQ ID NO: 163)
	SMS 47	20	CCGGGAGGGGGGGTCCTGGA (SEQ ID NO: 249)

2104649

- 52 -

	SMS 48	20	GGGGGTCCTGGAGGCTGCAC (SEQ ID NO: 370)
	SMS 49	17	GGAGGGGGGGTCCTGGA (SEQ ID NO: 246)
5	SMS 50	15	AGGGGGGGTCCTGGA (SEQ ID NO: 244)
	SMS 51	20	CAGAACCCGGACGCCATGCG (SEQ ID NO: 382)
10	SMS 52	16	GAACCCGGACGCCATG (SEQ ID NO: 376)
	SMS 53	20	GCGGGGGCAGCCCAAATCT (SEQ ID NO: 391)

In addition, the following antisense compounds were prepared as controls.

15	Name	Length (mer)	Sequence (5'-terminal to 3'-terminal)
	SMS 9	20	GTA GTTCCTCACAGGGGAGT (SEQ ID NO: 109; an antisense compound out of the scope of the claimed compounds.)
20	SMS 28	20	TGTGTTCTCCATGTTCCGGTG (SEQ ID NO: 393; derived from hepatitis virus B.)
25	SMS 29	20	GTCAATGTCCATGCCCCAAA (SEQ ID NO: 394; derived from hepatitis virus B.)
	SMS 31	20	GCGAGACTGCTAGCCGAGTA (SEQ ID NO: 395; the sense sequence corresponding to a region beginning from G at position 268 and ending at A at position 287 in SEQ ID NO: 1)
30	SMS 32	20	CCTCCAGAGCATCTGGCAGG (SEQ ID NO: 396; the inverted sequence of the complementary sequence to the region beginning from G at position 346 and ending at C at position 365 in SEQ ID NO: 1)
35			

- 5 SMS 33 16 GCGAGACTGCTAGCCG
(SEQ ID NO: 397; the sense sequence
corresponding to a region beginning from
G at position 268 and ending at G at
position 283 in SEQ ID NO: 1)
- 10 SMS 34 20 CATCACAACCCAGCGCTTTC
(SEQ ID NO: 398; the inverted sequence of
the complementary sequence to the region
beginning from G at position 285 and
ending at G at position 304 in SEQ ID
NO: 1)

The phosphate diester linkages between bases in
the above listed compounds are all phosphorothioate type.

- 15 (2) Measurement of inhibitory effect on intracellular
translation of the HCV-derived protein by antisense DNAs

- Human liver-derived cell line WRL68 which had
been cultivated on a 24-well plate to about 60% confluent
in TS-2 medium containing 10% fetal bovine serum was
infected at MOI = 0.01 PFU/cell for 1 hour at room
20 temperature with the recombinant vaccinia virus rVV5CL
which was mixed homogeneously with PBS containing 2% fetal
bovine serum. At the end of this period, the cells were
washed twice with 500 μ l of Opti-MEM medium, and then
cultivated in 500 μ l of Opti-MEM medium supplemented with
25 an antisense compound in a 5% CO₂ incubator at 37 °C for 16
hours. As described in Example 5 (3), after removal of the
medium, the infected cells were mixed with 500 μ l of
PicaGeneTM cell lysate solution, and allowed to stand for 30
min at room temperature. After mixing thoroughly, 8 μ l of

the mixture was added to 80 μ l of the color development solution, and ten seconds after, measured on MULTI-BIOLUMAT LB9505 (Berthold Japan) for 2.5 min at 27 °C. In order to create a calibration curve, a series of luciferase solutions diluted with PBS containing 1% BSA was prepared to have a concentration of 10^{-15} , 10^{-16} , 10^{-17} , 10^{-18} , or 10^{-19} mol/ μ l, and used as standard reagents. Each 8 μ l of these standard reagents was mixed with 80 μ l of the color development solution and measured as described above.

Since common logarithm of each luciferase concentration of standard reagents was a linear function of common logarithm of corresponding measurement (integrated value of the fluorescence), the linear line was used as a calibration curve.

The amount of luciferase expressed in the infected cells was determined from the measurement (integrated value of the fluorescence) using the calibration curve. The amount of luciferase thus determined was regarded as the amount of the fusion protein expressed from the fusion protein gene between the HCV-derived core protein and luciferase genes.

The expression of this fusion protein depends on the action of the region present in the 5' untranslated region of the HCV-derived gene which plays a role in HCV specific translation. IRES (Internal Ribosome Entry Site)

is believed to reside in this region. Ribosome may recognize the HCV-specific sequence and structure so that it binds at inner part, but not at the 5' end, of the mRNA to initiate the translation of the HCV protein (this function is referred as the IRES function). The fusion protein gene used herein contains sufficient region to express in infected cells the fusion protein between the HCV-derived core protein and the luciferase via such a function. Accordingly, the target region of antisense compounds is a HCV-derived gene sequence which takes part in the IRES function. Taking into account the fact that the IRES function arises from the mechanism by which the higher structure of RNA of the HCV gene is recognized, antisense compounds which may be capable of destroying such a higher structure were also selected.

In order to deduce the IRES of said gene, the secondary structure was analyzed with the analysis program FOLD (UWGCG Software, Univ. Wisconsin) on the basis of the RNA sequence beginning from the 5' untranslated region and ending at envelope 1 region of the HCV gene (corresponding to the base sequence from position 1 to position 1200 in SEQ ID NO: 1).

The results are shown in Figs. 4-6.

Among many antisense compounds designed herein, the antisense compounds particularly effective were those

directed to the sequences in the region beginning from thymine at position 107 and ending at adenine at position 199, such as Anti 1, SMS 3, SMS 11, SMS 18, SMS 22, SMS 30, SMS 35-37, SMS 44-50, and the like.

5 These antisense compounds were added to the medium of the infected cells at a final concentration of 5 μ M, 2.5 μ M, 1 μ M, 0.5 μ M, 0.25 μ M, 0.1 μ M, or 0.01 μ M.

10 The number of samples which can be assayed under the same conditions is limitary. Accordingly, in a signal run, 6 plates (24 well) were used at the most so that experimental conditions may be kept identical. The number of the antisense compounds and the number of concentration levels to be assayed at a time is limitative for this reason, and therefore, every run was conducted with some
15 wells (normally four wells) which are free from the antisense compound and a well which contains, in place of the antisense compound, a control compound (see Table 3) free from an activity possessed by the antisense compound. Although there was slight difference or variation among
20 experiments with respect to cell density, infection time, and cultivation time after infection, the amount of luciferase expressed in the presence of Anti 1, SMS 1, SMS 11, SMS 35, SMS 36, or SMS 37, was about from one tenth to about one twelfth of that expressed in the presence of an
25 antisense compound (SMS 9) which contains the sequence

derived from HCV, but which is hardly effective, or an antisense compound which does not contain HCV-derived sequence, such as SMS 28 or SMS 29. At the final concentration of 0.5 μ M, Anti 1, SMS 3, SMS 11, SMS 35, SMS 36, and SMS 37 reduced the expression about 30 to 50%.

When WRL 68 cells were cultured before infection with the recombinant vaccinia virus for 1.5-2.0 hours in OPTI-MEM medium (500 μ l), to which the antisense compound of the invention had been added so that the amount of the compound was identical to that used in the case where the antisense compound was added to the medium after the WRL 68 cells were infected with the recombinant vaccinia virus, the expression inhibition was increased. Thus, the antisense compounds, such as Anti 1, SMS 3, SMS 11, SMS 35, SMS 36, and SMS 37, showed about 90-100% translation inhibition at concentrations of 5 μ M, 2.5 μ M, and 1 μ M. In particular, Anti 1 was most effective (Fig. 6).

In summary, antisense compounds which require less than 1 μ M or even less than 0.5 μ M in order to exhibit about 50% or more inhibition of protein expression were discovered. It was also found that antisense compounds corresponding to a region other than a particular region in HCV polypeptide are definitely ineffective. It has been determined that said particular region corresponds to the base sequence from positions 107 to 199, preferably from

2104649

- 58 -

127 to 180, of the SEQ ID No. 1 of Sequence Listing. Thus,
it is believed that all of the target sequences of
antisense compounds are fallen within the above scope.

5 Because the antisense compounds of the present
invention act specifically on the mRNA of HCV to inhibit
the translation of HCV gene, they may be useful as an
antiviral agent against HCV.

2104649

- 59 -

SEQ ID NO:1

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 2033 base pairs

STRANDNESS: double

TOPOLOGY: linear

ANTI-SENSE: No

ORIGINAL SOURCE:

ORGANISM: Hepatitis C virus

IMMEDIATE SOURCE:

CLONE: T7N1-19

ACTAGTTAAT ACGACTCACT ATAGGGTGCC AGCCCCCTGA TGGGGGCGAC ACTCCACCAT 60
AGATCACTCC CCTGTGAGGA ACTACTGTCT TCACGCAGAA AGCGTCTAGC CATGGCGTTA 120
GTATGAGTGT CGTGCAGCCT CCAGGACCCC CCCTCCCGGG AGAGCCATAG TGGTCTGCGG 180
AACCGGTGAG TACACCGGAA TTGCCAGGAC GACCGGGTCC TTTCTTGGAT CAACCCGCTC 240
AATGCCTGGA GATTGGGGCG TGCCCCCGCG AGACTGCTAG CCGAGTAGTG TTGGGTCGCG 300
AAAGGCCTTG TGGTACTGCC TGATAGGGTG CTTGCGAGTG CCCCAGGAGG TCTCGTAGAC 360
CGTGCATC ATG AGC ACA AAT CCA AAA CCC CAA AGA AAA ATC AAA CGT AAC 410

Met Ser Thr Asn Pro Lys Pro Gln Arg Lys Ile Lys Arg Asn

1

5

10

ACC AAC CGC CGC CCA CAG GAC GTT AAG TTC CCG GGC GGT GGT CAG ATC 458

Thr Asn Arg Arg Pro Gln Asp Val Lys Phe Pro Gly Gly Gly Gln Ile

15

20

25

30

GTT GGT GGA GTT TAC CTG TTG CCG CGC AGG GGC CCC AGG TTG GGT GTG	506
Val Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly Pro Arg Leu Gly Val	
35 40 45	
CGC GCG ACT AGG AAG ACT TCC GAG CGG CCG CAA CCT CGT GGA AGG CGA	554
Arg Ala Thr Arg Lys Thr Ser Glu Arg Pro Gln Pro Arg Gly Arg Arg	
50 55 60	
CAA CCT ATC CCC AAG GCT CGC CAA CCC GAG GGT AGG GCC TGG GCT CAG	602
Gln Pro Ile Pro Lys Ala Arg Gln Pro Glu Gly Arg Ala Trp Ala Gln	
65 70 75	
CCC GGG TAC CCT TGG CCC CTC TAT GGC AAT GAG GGC TTG GGG TGG GCA	650
Pro Gly Tyr Pro Trp Pro Leu Tyr Gly Asn Glu Gly Leu Gly Trp Ala	
80 85 90	
GGA TGG CTC CTG TCA CCC CGC GGC TCC CGG CCT AGT TGG GGC CCC ACG	698
Gly Trp Leu Leu Ser Pro Arg Gly Ser Arg Pro Ser Trp Gly Pro Thr	
95 100 105 110	
GAC CCC CGG CGT AGG TCG CGT AAT TTG GGT AAG GTC ATC GAT ACC CTC	746
Asp Pro Arg Arg Arg Ser Arg Asn Leu Gly Lys Val Ile Asp Thr Leu	
115 120 125	
ACA TGC GGC TTC GCC GAC CTC ATG GGG TAC ATT CCG CTC GTC GGC GCC	794
Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile Pro Leu Val Gly Ala	
130 135 140	
CCC CTA GGG GGC GCT GCC AGG GCT CTA GCG CAT GGC GTC CGG GTT CTG	842
Pro Leu Gly Gly Ala Ala Arg Ala Leu Ala His Gly Val Arg Val Leu	
145 150 155	

2104649

- 61 -

GAG GAC GGC GTG AAC TAT GCA ACA GGG AAT CTG CCT GGT TGC TCC TTT	890
Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu Pro Gly Cys Ser Phe	
160 165 170	
TCT ATC TTC CTT TTG GCT TTG CTG TCC TGT TTG ACC ATC CCA GCT TCC	938
Ser Ile Phe Leu Leu Ala Leu Leu Ser Cys Leu Thr Ile Pro Ala Ser	
175 180 185 190	
GCC TAC CAA GTG CGC AAC GCG TCC GGG GTG TAC CAT GTC ACG AAC GAC	986
Ala Tyr Gln Val Arg Asn Ala Ser Gly Val Tyr His Val Thr Asn Asp	
195 200 205	
TGC TCC AAC TCA AGT ATT GTG TAT GAG GCG GCG GAC GTG ATT ATG CAC	1034
Cys Ser Asn Ser Ser Ile Val Tyr Glu Ala Ala Asp Val Ile Met His	
210 215 220	
ACC CCC GGG TGC GTG CCC TGC GTC CGG GAG AAC AAT TCC TCC CGC TGC	1082
Thr Pro Gly Cys Val Pro Cys Val Arg Glu Asn Asn Ser Ser Arg Cys	
225 230 235	
TGG GTA GCG CTC ACT CCC ACG CTT GCG GCC AGG AAC AGC AGC ATC CCC	1130
Trp Val Ala Leu Thr Pro Thr Leu Ala Ala Arg Asn Ser Ser Ile Pro	
240 245 250	
ACT ACG ACA ATA CGG CGT CAT GTC GAC TTG CTC GTT GGG GCA GCT GCT	1178
Thr Thr Thr Ile Arg Arg His Val Asp Leu Leu Val Gly Ala Ala Ala	
255 260 265 270	
CTC TGT TCC GCT ATG TAT GTG GGG GAT TTT TGC GGA TCT GTT TTC CTC	1226
Leu Cys Ser Ala Met Tyr Val Gly Asp Phe Cys Gly Ser Val Phe Leu	
275 280 285	

2104649

- 62 -

GTC TCC CAG CTG TTC ACT TTC TCA CCT CGC CGG TAT GAG ACG GTG CAA	1274
Val Ser Gln Leu Phe Thr Phe Ser Pro Arg Arg Tyr Glu Thr Val Gln	
290 295 300	
GAC TGC AAT TGC TCA ATC TAT CCC GGC CAT GTA TCA GGC CAT CGC ATG	1322
Asp Cys Asn Cys Ser Ile Tyr Pro Gly His Val Ser Gly His Arg Met	
305 310 315	
GCT TGG GAT ATG ATA ATG AAT TGG TCA CCT ACA ACA GCC CTA GTG GTA	1370
Ala Trp Asp Met Ile Met Asn Trp Ser Pro Thr Thr Ala Leu Val Val	
320 325 330	
TCG CAG CTA CTC CGG ATC CCA CAA GCC GTG GTG GAT ATG GTG GCA GGG	1418
Ser Gln Leu Leu Arg Ile Pro Gln Ala Val Val Asp Met Val Ala Gly	
335 340 345 350	
GCC CAC TGG GGA GTC CTG GCG GGC CTT GCC TAC TAT TCC ATG GTG GGG	1466
Ala His Trp Gly Val Leu Ala Gly Leu Ala Tyr Tyr Ser Met Val Gly	
355 360 365	
AAC TGG GCT AAG GTC TTG GTT GTG ATG CTG CTC TTC GCC GGT GTT GAC	1514
Asn Trp Ala Lys Val Leu Val Val Met Leu Leu Phe Ala Gly Val Asp	
370 375 380	
GGG GGG ACC CAC GTG ACA GGG GGG AAG GTA GCC TAC ACC ACC CAG GGC	1562
Gly Gly Thr His Val Thr Gly Gly Lys Val Ala Tyr Thr Thr Gln Gly	
385 390 395	
TTT ACA TCC TTC TTT TCA CGA GGG CCG TCT CAG AAA ATC CAA CTT GTA	1610
Phe Thr Ser Phe Phe Ser Arg Gly Pro Ser Gln Lys Ile Gln Leu Val	
400 405 410	

AAC ACT AAC GGC AGC TGG CAC ATC AAT AGG ACT GCC CTC AAT TGC AAT 1658
 Asn Thr Asn Gly Ser Trp His Ile Asn Arg Thr Ala Leu Asn Cys Asn
 415 420 425 430
 GAC TCC CTT AAC ACC GGG TTC CTT GCC GCG CTG TTC TAC ACC CAC AGC 1706
 Asp Ser Leu Asn Thr Gly Phe Leu Ala Ala Leu Phe Tyr Thr His Ser
 435 440 445
 TTC AAC GCG TCC GGA TGT CCG GAG CGT ATG GCC GGT TGC CGC CCC ATT 1754
 Phe Asn Ala Ser Gly Cys Pro Glu Arg Met Ala Gly Cys Arg Pro Ile
 450 455 460
 GAC GAG TTC GCT CAG GGG TGG GGT CCC ATC ACT CAT GTT GTG CCT AAC 1802
 Asp Glu Phe Ala Gln Gly Trp Gly Pro Ile Thr His Val Val Pro Asn
 465 470 475
 ATC TCG GAC CAG AGG CCC TAT TGC TGG CAC TAC GCG CCT CGA CCG TGT 1850
 Ile Ser Asp Gln Arg Pro Tyr Cys Trp His Tyr Ala Pro Arg Pro Cys
 480 485 490
 GGT ATC GTA CCC GCG TCG CAG GTG TGT GGT CCG GTG TAT TGC TTC ACC 1898
 Gly Ile Val Pro Ala Ser Gln Val Cys Gly Pro Val Tyr Cys Phe Thr
 495 500 505 510
 CCA AGC CCT GTT GTG GTG GGG ACG ACC GAT CGT TTC GGC GCC CCC ACG 1946
 Pro Ser Pro Val Val Val Gly Thr Thr Asp Arg Phe Gly Ala Pro Thr
 515 520 525
 TAC AAC TGG GGA AAC AAT GAG ACG GAT GTG CTA CTC CTC AAC AAC ACA 1994
 Tyr Asn Trp Gly Asn Asn Glu Thr Asp Val Leu Leu Leu Asn Asn Thr
 530 535 540

CGG CCG CCG CAG GGC AAC TGG TTC GGT TGT ACC TGG ATG
Arg Pro Pro Gln Gly Asn Trp Phe Gly Cys Thr Trp Met
545 550 555

2033

SEQ ID NO:2

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

TCCTGGAGGC TGCACG

16

SEQ ID NO:3

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GTCCTGGAGG CTGCACG

17

SEQ ID NO:4

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTCCTGGAG GCTGCACG

18

SEQ ID NO:5

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGTCTGGA GGCTGCACG

19

SEQ ID NO:6

SEQUENCE TYPE: nucleic acid

2104649

- 66 -

SEQUENCE LENGTH: 20 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR TYPE: other nucleic acid
ANTI-SENSE: Yes

GGGGTCCTGG AGGCTGCACG

20

SEQ ID NO:7
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 17 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR TYPE: other nucleic acid
ANTI-SENSE: Yes

TCCTGGAGGC TGCACGA

17

SEQ ID NO:8
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 18 base pairs
STRANDNESS: single
TOPOLOGY: linear

2104649

- 67 -

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GTCCTGGAGG CTGCACGA

18

SEQ ID NO:9

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTCCTGGAG GCTGCACGA

19

SEQ ID NO:10

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGTCCTGGA GGCTGCACGA

20

SEQ ID NO:11

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGGTCCTGG AGGCTGCACG A

21

SEQ ID NO:12

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

TCCTGGAGGC TGCACGAC

18

SEQ ID NO:13

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GTCTTGAGG CTGCACGAC

19

SEQ ID NO:14

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTCTTGAG GCTGCACGAC

20

SEQ ID NO:15

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

- 70 -

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGTCCTGGA GGCTGCACGA C

21

SEQ ID NO:16

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

ANTI-SENSE: Yes

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

GGGGTCCTGG AGGCTGCACG AC

22

SEQ ID NO:17

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCCTGGAGGC TGCACGACA

19

SEQ ID NO:18

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTCCTGGAGG CTGCACGACA

20

SEQ ID NO:19

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTCCTGGAG GCTGCACGAC A

21

SEQ ID NO:20

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGTCCTGGA GGCTGCACGA CA

22

SEQ ID NO:21

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGGTCCTGG AGGCTGCACG ACA

23

SEQ ID NO:22

SEQUENCE TYPE: nucleic acid

2104649

- 73 -

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCCTGGAGGC TGCACGACAC

20

SEQ ID NO:23

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTCCTGGAGG CTGCACGACA C

21

SEQ ID NO:24

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTCCTGGAG GCTGCACGAC AC

22

SEQ ID NO:25

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGTCCTGGA GGCTGCACGA CAC

23

SEQ ID NO:26

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGGGTCCTGG AGGCTGCACG ACAC

24

SEQ ID NO:27

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGGG AGGGG

15

SEQ ID NO:28

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGG

17

SEQ ID NO:29

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGG

19

SEQ ID NO:30

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG G

21

SEQ ID NO:31

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGG

24

SEQ ID NO:32

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGGG AGGGG

25

SEQ ID NO:33

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGG

15

SEQ ID NO:34

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGG

17

SEQ ID NO:35

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG

20

SEQ ID NO:36

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGGG AGGG

24

SEQ ID NO:37

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CAGACCACTA TGGCTCTCCC GGGAGGG

27

SEQ ID NO:38

SEQUENCE TYPE: nucleic acid

2104649

- 80 -

SEQUENCE LENGTH: 30 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGCAGACCA CTATGGCTCT CCCGGGAGGG

30

SEQ ID NO:39

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGCAGACCA CTATG

15

SEQ ID NO:40

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

2104649

- 81 -

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGCAGACCA CTATGGC

17

SEQ ID NO:41

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGCAGACCA CTATGGCTCT

20

SEQ ID NO:42

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

2104649

- 82 -

CCGCAGACCA CTATGGCTCT CCCG

24

SEQ ID NO:43

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGCAGACCA CTATGGCTCT CCCGGGA

27

SEQ ID NO:44

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CGACCCAACA CTACT

15

2104649

- 83 -

SEQ ID NO:45

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CGCGACCCAA CACTACT

17

SEQ ID NO:46

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TTTCGCGACC CAACACTACT

20

SEQ ID NO:47

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

2104649

- 84 -

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCGACCCAAC ACTAC

15

SEQ ID NO:48

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCGCGACCC AACACTAC

18

SEQ ID NO:49

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

2104649

- 85 -

ANTI-SENSE: Yes

CTTTCGCGAC CCAACACTAC

20

SEQ ID NO:50

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ACCACAAGGC CTTTC

15

SEQ ID NO:51

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ACCACAAGGC CTTTCGC

17

2104649

- 86 -

SEQ ID NO:52

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ACCACAAGGC CTTTCGCGAC

20

SEQ ID NO:53

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TACCACAAGG CCTTT

15

SEQ ID NO:54

SEQUENCE TYPE: nucleic acid

2104649

- 87 -

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TACCACAAGG CCTTTCG

17

SEQ ID NO:55

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TACCACAAGG CCTTTCGCGA

20

SEQ ID NO:56

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

AGTACCACAA GGCCT

15

SEQ ID NO:57

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

AGTACCACAA GGCCTTT

17

SEQ ID NO:58

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

2104649

- 89 -

AGTACCACAA GGCCTTTCGC

20

SEQ ID NO:59

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCTACGAGAC CTCCCGG

17

SEQ ID NO:60

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CGGTCTACGA GACCTCCCGG

20

2104649

- 90 -

SEQ ID NO:61

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCACGGTCTA CGAGACCTCC CGG

23 .

SEQ ID NO:62

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GATGCACGGT CTACGAGACC TCCCGG

26 .

SEQ ID NO:63

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTACGAGA CCTCCCGG

28

SEQ ID NO:64

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCATGATGCA CGGTCTACGA GACCTCCCGG

30

SEQ ID NO:65

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCTACGAGAC CTCCC

15

SEQ ID NO:66

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CGGTCTACGA GACCTCCC

18

SEQ ID NO:67

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCACGGTCTA CGAGACCTCC C

21

SEQ ID NO:68

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GATGCACGGT CTACGAGACC TCCC

24

SEQ ID NO:69

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTACGAGA CCTCCC

26

SEQ ID NO:70

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

TCATGATGCA CGGTCTACGA GACCTCCC

28

SEQ ID NO:71
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 29 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

CTCATGATGC ACGGTCTACG AGACCTCCC

29

SEQ ID NO:72
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 30 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTCTAC GAGACCTCCC

30

SEQ ID NO:73

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CGGTCTACGA GACCT

15

SEQ ID NO:74

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCACGGTCTA CGAGACCT

18

2104649

- 96 -

SEQ ID NO:75

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GATGCACGGT CTACGAGACC T

21

SEQ ID NO:76

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTACGAGA CCT

23

SEQ ID NO:77

SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 25 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

TCATGATGCA CGGTCTACGA GACCT

25

SEQ ID NO:78
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

CTCATGATGC ACGGTCTACG AGACCT

26

SEQ ID NO:79
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 27 base pairs
STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTCTAC GAGACCT

27

SEQ ID NO:80

SEQUENCE LENGTH: 29 base pairs

SEQUENCE TYPE: nucleic acid

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCACGGTCT ACGAGACCT

29

SEQ ID NO:81

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCACGGTCTA CGAGA

15

SEQ ID NO:82

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GATGCACGGT CTACGAGA

18

SEQ ID NO:83

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTACGAGA

20

2104649

- 100 -

SEQ ID NO:84

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCATGATGCA CGGTCTACGA GA

22

SEQ ID NO:85

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTCATGATGC ACGGTCTACG AGA

23

SEQ ID NO:86

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTCTAC GAGA

24

SEQ ID NO:87

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCACGGTCT ACGAGA

26

SEQ ID NO:88

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

2104649

- 102 -

ANTI-SENSE: Yes

ATGCACGGTC TACGA

15

SEQ ID NO:89

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTACGA

18

SEQ ID NO:90

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCATGATGCA CGGTCTACGA

20

2104649

- 103 -

SEQ ID NO:91

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTCATGATGC ACGGTCTACG A

21

SEQ ID NO:92

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTCTAC GA

22

SEQ ID NO:93

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

GTGCTCATGA TGCACGGTCT ACGA

24

SEQ ID NO:94
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 15 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

TGATGCACGG TCTAC

15

SEQ ID NO:95
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs
STRANDNESS: single
TOPOLOGY: linear

2104649

- 105 -

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

ATGATGCACG GTCTAC

16

SEQ ID NO:96

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCATGATGCA CGGTCTAC

18

SEQ ID NO:97

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTCATGATGC ACGGTCTAC

19

SEQ ID NO:98

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTCTAC

20

SEQ ID NO:99

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCACGGTCT AC

22

SEQ ID NO:100

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CTCATGATGC ACGGTC

16

SEQ ID NO:101

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGGTC

17

SEQ ID NO:102

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

2104649

- 108 -

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCACGGTC

19

SEQ ID NO:103

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GCTCATGATG CACGG

15

SEQ ID NO:104

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCACGG

17

SEQ ID NO:105

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GTGCTCATGA TGCAC

15

SEQ ID NO:106

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGG

19

SEQ ID NO:107

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TACTCACC GG TTCCGCAGAC CACTAT

26

SEQ ID NO:108

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TCATACTAAC GCCATGGCTA

20

SEQ ID NO:109

2104649

- 111 -

SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

GTAGTTCCTC ACAGGGGAGT

20

SEQ ID NO:110
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDNESS: single
TOPOLOGY: linear
MOLECULAR SEQUENCE TYPE: other nucleic acid
ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGG

20

SEQ ID NO:111
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDNESS: single

2104649

- 112 -

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

GGTTCGCAG ACCACTATGG

20

SEQ ID NO:112

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

TGGAGGCTGC ACGACACTCA

20

SEQ ID NO:113

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDNESS: single

TOPOLOGY: linear

MOLECULAR SEQUENCE TYPE: other nucleic acid

ANTI-SENSE: Yes

2104649

- 113 -

CAGTACCACA AGGCCTTTCG

20 .

SEQ ID NO: 114

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC ACGACAC

27 .

SEQ ID NO: 115

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CACGACAC

28 .

2104649

- 114 -

SEQ ID NO: 116

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCACGACAC

29

SEQ ID NO: 117

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCACGACAC

30

SEQ ID NO: 118

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

2104649

- 115 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC ACGACA

26

SEQ ID NO: 119

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CACGACA

27

SEQ ID NO: 120

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 116 -

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCACGACA

28

SEQ ID NO: 121

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCACGACA

29

SEQ ID NO: 122

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCACGACA

30

2104649

- 117 -

SEQ ID NO: 123
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 25 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC ACGAC

25

SEQ ID NO: 124
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CACGAC

26

SEQ ID NO: 125
SEQUENCE TYPE: nucleic acid

2104649

- 118 -

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCACGAC

27

SEQ ID NO: 126

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCACGAC

28

SEQ ID NO: 127

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

2104649

- 119 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCACGAC

29

SEQ ID NO: 128

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTGCACGAC

30

SEQ ID NO: 129

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC ACGA

24

SEQ ID NO: 130

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CACGA

25

SEQ ID NO: 131

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCACGA

26

2104649

- 121 -

SEQ ID NO: 132

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCACGA

27

SEQ ID NO: 133

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCACGA

28

SEQ ID NO: 134

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

2104649

- 122 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTGCACGA

29

SEQ ID NO: 135

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGGG GGGTCCTGGA GGCTGCACGA

30

SEQ ID NO: 136

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC ACG

23

SEQ ID NO: 137

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CACG

24

SEQ ID NO: 138

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCACG

25

2104649

- 124 -

SEQ ID NO: 139

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGG TCCTGGAGGC TGCACG

26

SEQ ID NO: 140

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCACG

27

SEQ ID NO: 141

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTGCACG

28

SEQ ID NO: 142
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 29 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CCGGGAGGGG GGCTCTGGA GGCTGCACG

29

SEQ ID NO: 143
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 30 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCCGGGAGGG GGGGTCCTGG AGGCTGCACG

30

SEQ ID NO: 144

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC AC

22

SEQ ID NO: 145

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CAC

23

SEQ ID NO: 146

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCAC

24

SEQ ID NO: 147

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCAC

25

SEQ ID NO: 148
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCAC

26

SEQ ID NO: 149
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 27 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTGCAC

27

SEQ ID NO: 150
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGCTGCAC

28

SEQ ID NO: 151

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGTCCTGG AGGCTGCAC

29

SEQ ID NO: 152

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

- 130 -

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCTG GAGGCTGCAC

30

SEQ ID NO: 153

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC A

21

SEQ ID NO: 154

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG CA

22

SEQ ID NO: 155

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GCA

23

SEQ ID NO: 156

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGCA

24

SEQ ID NO: 157

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGCA

25

SEQ ID NO: 158

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTGCA

26

SEQ ID NO: 159

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESSSS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

- 133 -

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGCTGCA

27

SEQ ID NO: 160

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGGTCCTGG AGGCTGCA

28

SEQ ID NO: 161

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGTCCTG GAGGCTGCA

29

SEQ ID NO: 162

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTCCT GGAGGCTGCA

30

SEQ ID NO: 163

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTGC

20

SEQ ID NO: 164

SEQUENCE TYPE: nucleic acid

- 135 -

SEQUENCE LENGTH: 21 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG C

21

SEQ ID NO: 165
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 22 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT GC

22

SEQ ID NO: 166
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 23 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

- 136 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TGC

23

SEQ ID NO: 167

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTGC

24

SEQ ID NO: 168

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 137 -

CGGGAGGGGG GGTCTGGAG GCTGC

25

SEQ ID NO: 169

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGCTGC

26

SEQ ID NO: 170

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGTCCTGG AGGCTGC

27

SEQ ID NO: 171

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCTG GAGGCTGC

28

SEQ ID NO: 172

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGTCCT GGAGGCTGC

29

SEQ ID NO: 173

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TGGAGGCTGC

30

SEQ ID NO: 174

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCTG

19

SEQ ID NO: 175

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCTG

20

SEQ ID NO: 176

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT G

21

SEQ ID NO: 177

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC TG

22

2104649

- 141 -

SEQ ID NO: 178
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 23 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CTG

23

SEQ ID NO: 179
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 24 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCTG

24

SEQ ID NO: 180
SEQUENCE TYPE: nucleic acid

2104649

- 142 -

SEQUENCE LENGTH: 25 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGCTG

25

SEQ ID NO: 181
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CCCGGGAGGG GGGGTCCTGG AGGCTG

26

SEQ ID NO: 182
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 27 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

2104649

- 143 -

MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TCCCCGGGAGG GGGGGTCCTG GAGGCTG

27

SEQ ID NO: 183
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 28 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCCCCGGGAG GGGGGTCCT GGAGGCTG

28

SEQ ID NO: 184
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 29 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

2104649

- 144 -

TCTCCCGGA GGGGGGTCC TGGAGGCTG

29

SEQ ID NO: 185

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGTC CTGGAGGCTG

30

SEQ ID NO: 186

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGCT

18

SEQ ID NO: 187

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGGCT

19

SEQ ID NO: 188

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGCT

20

SEQ ID NO: 189

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC T

21

SEQ ID NO: 190

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG CT

22

SEQ ID NO: 191

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 147 -

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GCT

23

SEQ ID NO: 192

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGCT

24

SEQ ID NO: 193

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGAGGG GGGTCCTGG AGGCT

25

2104649

- 148 -

SEQ ID NO: 194

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCTG GAGGCT

26

SEQ ID NO: 195

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGTCCT GGAGGCT

27

SEQ ID NO: 196

SEQUENCE TYPE: nucleic acid

2104649

- 149 -

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TGGAGGCT

28

SEQ ID NO: 197

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGGG AGGGGGGGTC CTGGAGGCT

29

SEQ ID NO: 198

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

2104649

- 150 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCTGGAGGCT

30

SEQ ID NO: 199

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGGC

17

SEQ ID NO: 200

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 151 -

AGGGGGGGTC CTGGAGGC

18

SEQ ID NO: 201

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGGC

19

SEQ ID NO: 202

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAGGC

20

2104649

- 152 -

SEQ ID NO: 203
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 21 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG C

21

SEQ ID NO: 204
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 22 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG GC

22

SEQ ID NO: 205
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 23 base pairs

2104649

- 153 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GGC

23

SEQ ID NO: 206

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGTCCTGG AGGC

24

SEQ ID NO: 207

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 154 -

ANTI-SENSE: Yes

TCCCCGGGAGG GGGGGTCCTG GAGGC

25

SEQ ID NO: 208

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCCGGGAG GGGGGTCCT GGAGGC

26

SEQ ID NO: 209

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCCGGA GGGGGGTCC TGGAGGC

27

2104649

- 155 -

SEQ ID NO: 210
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 28 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCTCCCGGG AGGGGGGGTC CTGGAGGC

28

SEQ ID NO: 211
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 29 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCTGGAGGC

29

SEQ ID NO: 212
SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TCCTGGAGGC

30

SEQ ID NO: 213

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGGGTCC TGGAGG

16

SEQ ID NO: 214

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

2104649

- 157 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

AGGGGGGGTC CTGGAGG

17

SEQ ID NO: 215

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE T: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAGG

18

SEQ ID NO: 216

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 158 -

GGAGGGGGGG TCCTGGAGG

19

SEQ ID NO: 217

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGAGG

20

SEQ ID NO: 218

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG G

21

2104649

- 159 -

SEQ ID NO: 219

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTGGA GG

22

SEQ ID NO: 220

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGGTCCTGG AGG

23

SEQ ID NO: 221

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

2104649

- 160 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCCGGGAGG GGGGGTCCTG GAGG

24

SEQ ID NO: 222

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCCGGGAG GGGGGTCCT GGAGG

25

SEQ ID NO: 223

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 161 -

ANTI-SENSE: Yes

TCTCCCGGA GGGGGGTCC TGGAGG

26

SEQ ID NO: 224

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGTC CTGGAGG

27

SEQ ID NO: 225

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGT CCTGGAGG

28

2104649

- 162 -

SEQ ID NO: 226

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TCCTGGAGG

29

SEQ ID NO: 227

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCTGGAGG

30

SEQ ID NO: 228

SEQUENCE TYPE: nucleic acid

2104649

- 163 -

SEQUENCE LENGTH: 15 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGGGGGTCC TGGAG

15

SEQ ID NO: 229
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

AGGGGGGGTC CTGGAG

16

SEQ ID NO: 230
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 17 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

2104649

- 164 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GAGGGGGGGT CCTGGAG

17

SEQ ID NO: 231

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGAG

18

SEQ ID NO: 232

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

2104649

- 165 -

GGGAGGGGGG GTCCTGGAG

19

SEQ ID NO: 233

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGAG

20

SEQ ID NO: 234

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGTCTGGA G

21

- 166 -

SEQ ID NO: 235

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCCGGGAGGG GGGGTCCTGG AG

22

SEQ ID NO: 236

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCCGGGAGG GGGGGTCCTG GAG

23

SEQ ID NO: 237

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

2104649

- 167 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTCCT GGAG

24

SEQ ID NO: 238

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TGGAG

25

SEQ ID NO: 239

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 168 -

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGGTC CTGGAG

26

SEQ ID NO: 240

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCTGGAG

27

SEQ ID NO: 241

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGGG TCCTGGAG

28

SEQ ID NO: 242
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 29 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCTGGAG

29

SEQ ID NO: 243
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 30 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGTCTGGAG

30

SEQ ID NO: 244
SEQUENCE TYPE: nucleic acid

- 170 -

SEQUENCE LENGTH: 15 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

AGGGGGGGTC CTGGA

15

SEQ ID NO: 245
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAGGGGGGGT CCTGGA

16

SEQ ID NO: 246
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 17 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

- 171 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTGGA

17

SEQ ID NO: 247

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGGA

18

SEQ ID NO: 248

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTGGA

19

SEQ ID NO: 249

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGAGGGGG GGTCTGGA

20

SEQ ID NO: 250

SEQUENCE LENGTH: 21 base pairs

SEQUENCE TYPE: nucleic acid

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGAGGG GGGTCTGG A

21

SEQ ID NO: 251
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 22 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCTG GA

22

SEQ ID NO: 252
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 23 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTCCT GGA

23

SEQ ID NO: 253
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TGGA

24

SEQ ID NO: 254

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGGG AGGGGGGGTC CTGGA

25

SEQ ID NO: 255

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCTGGA

26

SEQ ID NO: 256

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TCCTGGA

27

SEQ ID NO: 257

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCTGGA

28

SEQ ID NO: 258

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGTCTGGA

29

SEQ ID NO: 259

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGGG GGGTCCTGGA

30

SEQ ID NO: 260

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAGGGGGGGT CCTGG

15

SEQ ID NO: 261
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGAGGGGGGG TCCTGG

16

SEQ ID NO: 262
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 17 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTGG

17

SEQ ID NO: 263

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGCCTGG

18

SEQ ID NO: 264

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGGTCCTGG

20

SEQ ID NO: 265

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCTG G

21

SEQ ID NO: 266

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGTCCT GG

22

SEQ ID NO: 267

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TGG

23

SEQ ID NO: 268

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGGG AGGGGGGGTC CTGG

24

SEQ ID NO: 269

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

2104649

- 181 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCTGG

25

SEQ ID NO: 270

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGGG TCCTGG

26

SEQ ID NO: 271

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCTGG

27

SEQ ID NO: 272

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGTCTGG

28

SEQ ID NO: 273

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGG GGTCTGG

29

- 183 -

SEQ ID NO: 274

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGGTCCTGG

30

SEQ ID NO: 275

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGAGGGGGGG TCCTG

15

SEQ ID NO: 276

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGAGGGGGG GTCCTG

16

SEQ ID NO: 277

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTG

17

SEQ ID NO: 278

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCCTG

18

SEQ ID NO: 279

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGTCCTG

19

SEQ ID NO: 280

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGTCCTG

20

SEQ ID NO: 281
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 21 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTCCT G

21

SEQ ID NO: 282
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 22 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGTCC TG

22

SEQ ID NO: 283
SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGTC CTG

23

SEQ ID NO: 284

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGT CCTG

24

SEQ ID NO: 285

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

2104649

- 188 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TCCTG

25

SEQ ID NO: 286

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCTG

26

SEQ ID NO: 287

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGGCTCTCC CGGGAGGGGG GGTCTTG

27

SEQ ID NO: 288

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGG GGGTCCTG

28

SEQ ID NO: 289

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGTCCTG

29

2104619

- 190 -

SEQ ID NO: 290
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 30 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGGTCCTG

30

SEQ ID NO: 291
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 15 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGGAGGGGGG GTCCT

15

SEQ ID NO: 292
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs

2104649

- 191 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCTT

16

SEQ ID NO: 293

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGGG GGGTCCT

17

SEQ ID NO: 294

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 192 -

ANTI-SENSE: Yes

CCCCGGGAGGG GGGGTCCT

18

SEQ ID NO: 295

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTCCT

19

SEQ ID NO: 296

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGTCCT

20

SEQ ID NO: 297

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGA GGGGGGTCC T

21

SEQ ID NO: 298

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGTC CT

22

SEQ ID NO: 299

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CCT

23

SEQ ID NO: 300

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGGG TCCT

24

SEQ ID NO: 301

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 195 -

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCCT

25

SEQ ID NO: 302

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGCCT

26

SEQ ID NO: 303

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGG GGGTCCT

27

2104649

- 196 -

SEQ ID NO: 304

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGGTCCT

28

SEQ ID NO: 305

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGTCCT

29

SEQ ID NO: 306

SEQUENCE TYPE: nucleic acid

2104649

- 197 -

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGGGGGTCCT

30

SEQ ID NO: 307

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGGGAGGGGG GGTCC

15

SEQ ID NO: 308

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTCC

16

SEQ ID NO: 309

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGTCC

17

SEQ ID NO: 310

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 199 -

TCCCGGGAGG GGGGGTCC

18

SEQ ID NO: 311

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTCC

19

SEQ ID NO: 312

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGTCC

20

SEQ ID NO: 313

SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 21 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGGTC C

21

SEQ ID NO: 314
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 22 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT CC

22

SEQ ID NO: 315
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 23 base pairs
STRANDEDNESS: single

- 201 -

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TCC

23

SEQ ID NO: 316

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTCC

24

SEQ ID NO: 317

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGTCC

25

SEQ ID NO: 318
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGG GGGTCC

26

SEQ ID NO: 319
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 27 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGGTCC

27

SEQ ID NO: 320

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGGTCC

28

SEQ ID NO: 321

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGGGGTCC

29

SEQ ID NO: 322

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCACTATGGC TCTCCCGGGA GGGGGGGTCC

30 .

SEQ ID NO: 323

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCGGGAGGGG GGGTC

15 .

SEQ ID NO: 324

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGGTC

16

SEQ ID NO: 325

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGTC

17

SEQ ID NO: 326

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGTC

18

SEQ ID NO: 327

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGA GGGGGGTC

19

SEQ ID NO: 328

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGTC

20

SEQ ID NO: 329

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

2104649

- 207 -

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGGT C

21

SEQ ID NO: 330

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGG TC

22

SEQ ID NO: 331

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GTC

23

SEQ ID NO: 332

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GGTC

24

SEQ ID NO: 333

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGGAGGGG GGGTC

25

2104649

- 209 -

SEQ ID NO: 334

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGGTC

26

SEQ ID NO: 335

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGGTC

27

SEQ ID NO: 336

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGGGGGTC

28

SEQ ID NO: 337

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCACTATGGC TCTCCCGGGA GGGGGGGTC

29

SEQ ID NO: 338

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

2104649

- 211 -

ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGGG AGGGGGGGTC

30

SEQ ID NO: 339

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGGAGGG GGGGT

15

SEQ ID NO: 340

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGGT

16

SEQ ID NO: 341
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 17 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CTCCCGGGAG GGGGGGT

17

SEQ ID NO: 342
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 18 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

TCTCCCGGGA GGGGGGGT

18

SEQ ID NO: 343
SEQUENCE TYPE: nucleic acid

- 213 -

SEQUENCE LENGTH: 19 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGGT

19

SEQ ID NO: 344

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGT

20

SEQ ID NO: 345

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 21 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

2104649

- 214 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGGG T

21

SEQ ID NO: 346

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG GT

22

SEQ ID NO: 347

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 215 -

ATGGCTCTCC CGGGAGGGG GGT

23

SEQ ID NO: 348

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TATGGCTCTC CCGGAGGGG GGGT

24

SEQ ID NO: 349

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGT

25

- 216 -

SEQ ID NO: 350

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 26 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGGT

26

SEQ ID NO: 351

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 27 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGGGGT

27

SEQ ID NO: 352

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCACTATGGC TCTCCCGGGA GGGGGGGT

28

SEQ ID NO: 353

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGGG AGGGGGGGT

29

SEQ ID NO: 354

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

- 218 -

ANTI-SENSE: Yes

GACCACTATG GCTCTCCCGG GAGGGGGGGT

30

SEQ ID NO: 355

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCCCGGGAGG GGGGG

15

SEQ ID NO: 356

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCCCGGGAG GGGGGG

16

- 219 -

SEQ ID NO: 357

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TCTCCCGGA GGGGGG

17

SEQ ID NO: 358

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTCTCCCGG AGGGGGG

18

SEQ ID NO: 359

SEQUENCE TYPE: nucleic acid

2104649

- 220 -

SEQUENCE LENGTH: 19 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GCTCTCCCGG GAGGGGGGG

19

SEQ ID NO: 360
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GGCTCTCCCG GGAGGGGGGG

20

SEQ ID NO: 361
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 21 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

2104649

- 221 -

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGGCTCTCCC GGGAGGGGGG G

21

SEQ ID NO: 362

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ATGGCTCTCC CGGGAGGGGG GG

22

SEQ ID NO: 363

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 23 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

- 222 -

TATGGCTCTC CCGGGAGGGG GGG

23

SEQ ID NO: 364

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 24 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CTATGGCTCT CCCGGGAGGG GGGG

24

SEQ ID NO: 365

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACTATGGCTC TCCCGGGAGG GGGGG

25

- 223 -

SEQ ID NO: 366
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 26 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CACTATGGCT CTCCCGGGAG GGGGGG

26

SEQ ID NO: 367
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 27 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CCACTATGGC TCTCCCGGGA GGGGGG

27

SEQ ID NO: 368
SEQUENCE LENGTH: 28 base pairs
SEQUENCE TYPE: nucleic acid

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

ACCACTATGG CTCTCCCGG AGGGGGGG

28

SEQ ID NO: 369

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 29 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GACCACTATG GCTCTCCCGG GAGGGGGGG

29

SEQ ID NO: 370

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GGGGGTCCTG GAGGCTGCAC

20

SEQ ID NO: 371

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGACGCC ATGCC

15

SEQ ID NO: 372

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGACGCC ATGCGCT

17

- 226 -

SEQ ID NO: 373

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGACGCC ATGCGCTAGA

20

SEQ ID NO: 374

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCCGGACGCC ATGCGCTAGA GCCCT

25

SEQ ID NO: 375

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

CCCGGACGCC ATGCGCTAGA GCCCTGGCAG

30

SEQ ID NO: 376
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 16 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAACCCGGAC GCCATG

16

SEQ ID NO: 377
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDEDNESS: single
TOPOLOGY: linear

2104649

- 228 -

MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAACCCGGAC GCCATGCGCT

20

SEQ ID NO: 378
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 25 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAACCCGGAC GCCATGCGCT AGAGC

25

SEQ ID NO: 379
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 30 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GAACCCGGAC GCCATGCGCT AGAGCCCTGG

30

SEQ ID NO: 380

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 15 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CAGAACCCGG ACGCC

15

SEQ ID NO: 381

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 18 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CAGAACCCGG ACGCCATG

18

- 230 -

SEQ ID NO: 382

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CAGAACCCGG ACGCCATGCG

20

SEQ ID NO: 383

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CAGAACCCGG ACGCCATGCG CTAGA

25

SEQ ID NO: 384

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

2104649

- 231 -

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CAGAACCCGG ACGCCATGCG CTAGAGCCCT

30

SEQ ID NO: 385

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGTCCTCCAG AACCCGGACG

20

SEQ ID NO: 386

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

- 232 -

ANTI-SENSE: Yes

CGTCCTCCAG AACCCGGACG CCATG

25

SEQ ID NO: 387

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CGTCCTCCAG AACCCGGACG CCATGCGCTA

30

SEQ ID NO: 388

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACGCCGTCC TCCAGAACCC GGACG

25

SEQ ID NO: 389

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CACGCCGTCC TCCAGAACCC GGACGCCATG

30

SEQ ID NO: 390

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 30 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TAGTTCACGC CGTCCTCCAG AACCCGGACG

30

SEQ ID NO: 391

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes

GCGGGGGCAC GCCCAAATCT

20

SEQ ID NO: 392
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 19 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid
ANTI-SENSE: Yes
AAGGGTGGGG GGGAAACGG

19

SEQ ID NO: 393
SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 20 base pairs
STRANDEDNESS: single
TOPOLOGY: linear
MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

TGTGTTCTCC ATGTTGCGTG

20

SEQ ID NO: 394

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GTCAATGTCC ATGCCCCAAA

20

SEQ ID NO: 395

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCGAGACTGC TAGCCGAGTG

20

SEQ ID NO: 396

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CCTCCAGAGC ATCTGGCACG

20

SEQ ID NO: 397

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

GCGAGACTGC TAGCCG

16

SEQ ID NO: 398

SEQUENCE TYPE: nucleic acid

- 237 -

SEQUENCE LENGTH: 20 base pairs

STRANDEDNESS: single

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid

ANTI-SENSE: Yes

CATCACAACC CAGCGCTTTC

20

SEQ ID NO: 399

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

GTAAAACGAC GGCCAGT

17

SEQ ID NO: 400

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CAGGAAACAG CTATGAC

17

SEQ ID NO: 401

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 16 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CAGATCTGCA AGCTTG

16

SEQ ID NO: 402

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CAGGAAACAG CTATGAC

17

SEQ ID NO: 403

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

GAATAGTTTT TCAATTTTGA CG

22

SEQ ID NO: 404

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 22 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CGTAAAAATT GAAAAACTAT TC

22

SEQ ID NO: 405

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 17 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

GTAAAACGAC GGCCAGT

17

SEQ ID NO: 406

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 40 base pairs

TOPOLOGY: linear

- 240 -

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

GATCCAAAAA TTGAAAAACT AGTCTAATTT ATTGCACGGA

40

GTTTTT AACTTTTTGA TCAGATTAAA TAACGTGCCT CTAG

SEQ ID NO: 407

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 25 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CGAAGCTTGCC AGCCCCCTGA TGGG

25

SEQ ID NO: 408

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 28 base pairs

TOPOLOGY: linear

MOLECULE SEQUENCE TYPE: Other nucleic acid, synthetic DNA

CCGGATCCCG GAAGCTGGGA TGGTCAAC

28

SEQ ID NO: 409

SEQUENCE TYPE: nucleic acid
SEQUENCE LENGTH: 2360 base pairs
STRANDEDNESS: double
TOPOLOGY: linear
ORIGINAL SOURCE
ORGANISM: Vaccinia virus
IMMEDIATE SOURCE
CLONE: PHASE

TCGACGATTG TTCATGATGG CAAGATTTAT ATATCTGGAG GTTACAACAA TAGTAGTGTA	60
GTTAATGTAA TATCGAATCT AGTCCTTAGC TATAATCCGA TATATGATGA ATGGACCAAA	120
TTATCATCAT TAAACATTCC TAGAATTAAT CCCGCTCTAT GGTCAGCGCA TAATAAATTA	180
TATGTAGGAG GAGGAATATC TGATGATGTT CGAACTAATA CATCTGAAAC ATACGATAAA	240
GAAAAAGATT GTTGGACATT GGATAATGGT CACGTGTTAC CACGCAATTA TATAATGTAT	300
AAATGCGAAC CGATTAAACA TAAATATCCA TTGGAAAAAA CACGTACAC GAATGATTTT	360
CTAAAGTATT TGGAAAGTTT TATAGGTAGT TGATAGAACA AAATACATAA TTTTGTAATA	420
ATAAATCACT TTTTATACTA ATATGACACG ATTACCAATA CTTTGTGTAC TAATATCATT	480
AGTATACGCT ACACCTTTTC CTCAGACATC TAAAAAATA GGTGATGATG CAACTCTATC	540
ATGTAATCGA AATAATACAA ATGACTACGT TGTATGAGT GCTTGGTATA AGGAGCCCAA	600
TTCCATTATT CTTTGTAGCTG CTAAAAGCGA CGTCTTGAT TTTGATAATT ATACCAAGGA	660
TAAATATCT TACGACTCTC CATACGATGA TCTAGTTACA ACTATCACAA TTAAATCATT	720
GACTGCTAGA GATGCCGGTA CTTATGTATG TGCATTCTTT ATGACATCAA CTACAAATGA	780
CACTGATAAA GTAGATTATG AAGAATACTC CACAGAGTTG ATTGTAAATA CAGATAGTGA	840
ATCGACTATA GACATAATAC TATCTGGATC TACACATTCA CCAGAACTA GCTAGTTCTG	900
AGAAACCAGA GGATATAGAT AATTTTAATT GCTCGTCGGT ATTCGAAATC GGGTCGACAT	960

CTATATACTA	TATAGTAATA	CCAATACTCA	AGACTACGAA	ACTGATACAA	TCTCTTATCA	1020
TGTGGGTAAT	GTTCTCGATG	TCGATAGCCA	TATGCCCGGT	AGTTGCGATA	TACATAAACT	1080
GATCACTAAT	TCCAAACCCA	CCCACTTTTT	ATAGTAAGTT	TTTCACCCAT	AAATAATAAA	1140
TACAATAATT	AATTTCTCGT	AAAAATTGAA	AACTATTCT	AATTTATTGC	ACGGTAAGGA	1200
AGTAGAATCA	TAAAGAACAG	TGACTCTAGA	GGATCCAAAA	ATTGAAAAAC	TAGTCTAATT	1260
TATTGCACGG	AGATCCAAAA	ATTGAAAAAC	TAGTCTAATT	TATTGCACGG	AGATCCAAAA	1320
ATTGAAAAAC	TAGTCTAATT	TATTGCACGG	AGATCCAAAA	ATTGAAAAAC	TAGTCTAATT	1380
TATTGCACGG	AGATCCAAAA	ATTGAAAAAC	TAGTCTAATT	TATTGCACGG	AGATCCAAAA	1440
ATTGAAAAAC	TAGTCTAATT	TATTGCACGG	AGATCTGCAA	GCTTGGGGTA	CCGAGCTCGA	1500
ATTCGACTCC	GGAACCAATT	ACTGATAATG	TAGAAGATCA	TACAGACACC	GTCACATACA	1560
CTAGCTAGTG	ATAGCATTAA	TACAGTAAGT	GCATCATCTG	GAGAATCCAC	AACAGACGAG	1620
ACTCCGGAAC	CAATTACTGA	TAAAGAAGAA	GATCATACAG	TCACAGACAC	TGTCTCATAC	1680
ACTACAGTAA	GTACATCATC	TGGAATTGTC	ACTACTAAAT	CAACCACCGA	TGATGCGGAT	1740
CTTTATGATA	CGTACAATGA	TAATGATACA	GTACCACCAA	CTACTGTAGG	CGGTAGTACA	1800
ACCTCTATTA	GCAATTATAA	AACCAAGGAC	TTTGTAGAAA	TATTTGGTAT	TACCGCATTA	1860
ATTATATTGT	CGGCCGTGGC	AATATTCTGT	ATTACATATT	ATATATATAA	TAAACGTTCA	1920
CGTAAATACA	AAACAGAGAA	CAAAGTCTAG	ATTTTGTACT	TACATAAATG	TCTGGGATAG	1980
TAAAATCTAT	CATATTGAGC	GGACCATCTG	GTTTCAGGAA	GACAGCCATA	GCCAAAAGAC	2040
TATGGGAATA	TATTTGGATT	TGTGGTGTCC	CATACCACTA	GATTTCCCTG	TCCTATGGAA	2100
CGAGAAGGTG	TCGATTACCA	TTACGTTAAC	AGAGAGGCCA	TCTGGAAGGG	AATAGCCGCC	2160
GGAAACTTTC	TAGAACATAC	TGAGTTTTTA	GGAAATATTT	ACGGAAC TTC	TAAAACTGCT	2220
GTGAATACAG	CGGCTATTAA	TAATCGTATT	TGTGTGATGG	ATCTAAACAT	CGATGGCGTT	2280
AGAAGTCTTA	AAAATACGTA	CCTAATGCCT	TACTCGGTGT	ATATAAGACC	TACCTCTCTT	2340
AAAATGGTTG	AGACCAAGCT					2360

2104649

- 243 -

SEQ ID NO: 410

SEQUENCE TYPE: nucleic acid

SEQUENCE LENGTH: 4987 base pairs

STRANDEDNESS: double

TOPOLOGY: linear

ORIGINAL SOURCE

ORGANISM: Vaccinia virus, Hepatitis C virus, Firefly luciferase gene

IMMEDIATE SOURCE

CLONE: pHA5CL

TCGACGATTG	TTCATGATGG	CAAGATTTAT	ATATCTGGAG	GTTACAACAA	TAGTAGTGTA	60
GTTAATGTAA	TATCGAATCT	AGTCCTTAGC	TATAATCCGA	TATATGATGA	ATGGACCAAA	120
TTATCATCAT	TAAACATTCC	TAGAATTAAT	CCCGCTCTAT	GGTCAGCGCA	TAATAAATTA	180
TATGTAGGAG	GAGGAATATC	TGATGATGTT	CGAACTAATA	CATCTGAAAC	ATACGATAAA	240
GAAAAAGATT	GTTGGACATT	GGATAATGGT	CACGTGTTAC	CACGCAATTA	TATAATGTAT	300
AAATGCGAAC	CGATTAAACA	TAAATATCCA	TTGGAAAAAA	CACAGTACAC	GAATGATTTT	360
CTAAAGTATT	TGGAAAGTTT	TATAGGTAGT	TGATAGAACA	AAATACATAA	TTTTGTAAAA	420
ATAAATCACT	TTTTATACTA	ATATGACACG	ATTACCAATA	CTTTTGTTAC	TAATATCATT	480
AGTATACGCT	ACACCTTTTC	CTCAGACATC	TAAAAAATA	GGTGATGATG	CAACTCTATC	540
ATGTAATCGA	AATAATACAA	ATGACTACGT	TGTTATGAGT	GCTTGGTATA	AGGAGCCCAA	600
TTCCATTATT	CTTTTAGCTG	CTAAAAGCGA	CGTCTTGAT	TTTGATAATT	ATACCAAGGA	660
TAAAATATCT	TACGACTCTC	CATACGATGA	TCTAGTTACA	ACTATCACAA	TTAAATCATT	720
GACTGCTAGA	GATGCCGGTA	CTTATGTATG	TGCATTCTTT	ATGACATCAA	CTACAAATGA	780
CACTGATAAA	GTAGATTATG	AAGAATACTC	CACAGAGTTG	ATTGTAAATA	CAGATAGTGA	840
ATCGACTATA	GACATAATAC	TATCTGGATC	TACACATTCA	CCAGAAACTA	GCTAGTTCTG	900

AGAAACCAGA GGATATAGAT AATTTTAATT GCTCGTCGGT ATTCGAAATC GGGTCGACAT 960
 CTATATACTA TATAGTAATA CCAATACTCA AGACTACGAA ACTGATACAA TCTCTTATCA 1020
 TGTGGGTAAT GTTCTCGATG TCGATAGCCA TATGCCCCGGT AGTTGCGATA TACATAAACT 1080
 GATCACTAAT TCCAAACCCA CCCACTTTTT ATAGTAAGTT TTTCACCCAT AAATAATAAA 1140
 TACAATAATT AATTTCTCGT AAAAATTGAA AACTATTCT AATTTATTGC ACGGTAAGGA 1200
 AGTAGAATCA TAAAGAACAG TGA CTCTAGA GGATCCAAAA ATTGAAAAAC TAGTCTAATT 1260
 TATTGCACGG AGATCCAAAA ATTGAAAAAC TAGTCTAATT TATTGCACGG AGATCCAAAA 1320
 ATTGAAAAAC TAGTCTAATT TATTGCACGG AGATCCAAAA ATTGAAAAAC TAGTCTAATT 1380
 TATTGCACGG AGATCCAAAA ATTGAAAAAC TAGTCTAATT TATTGCACGG AGATCCAAAA 1440
 ATTGAAAAAC TAGTCTAATT TATTGCACGG AGATCTGCAA GCTTGCCAGC CCCCTGATGG 1500
 GGGCGACACT CCACCATAGA TCACTCCCCT GTGAGGAACT ACTGTCTTCA CGCAGAAAGC 1560
 GTCTAGCCAT GCGGTTAGTA TGAGTGTCTG GCAGCCTCCA GGACCCCCC TCCCGGGAGA 1620
 GCCATAGTGG TCTGCGGAAC CGGTGAGTAC ACCGGAATTG CCAGGACGAC CGGGTCCTTT 1680
 CTTGGATCAA CCCGCTCAAT GCCTGGAGAT TTGGGCGTGC CCCC GCGAGA CTGCTAGCCG 1740
 AGTAGTGTG GGTGCGGAAA GGCCTTGTGG TACTGCCTGA TAGGGTGCTT GCGAGTGCCC 1800
 CGGGAGGTCT CGTAGACCGT GCATC ATG AGC ACA AAT CCA AAA CCC CAA AGA 1852

Met Ser Thr Asn Pro Lys Pro Gln Arg

1

5

AAA ATC AAA CGT AAC ACC AAC CGC CGC CCA CAG GAC GTT AAG TTC CCG 1900
 Lys Ile Lys Arg Asn Thr Asn Arg Arg Pro Gln Asp Val Lys Phe Pro
 10 15 20 25
 GGC GGT GGT CAG ATC GTT GGT GGA GTT TAC CTG TTG CCG CGC AGG GGC 1948
 Gly Gly Gly Gln Ile Val Gly Gly Val Tyr Leu Leu Pro Arg Arg Gly
 30 35 40

2104649

- 245 -

CCC AGG TTG GGT GTG CGC GCG ACT AGG AAG ACT TCC GAG CGG CCG CAA	1996
Pro Arg Leu Gly Val Arg Ala Thr Arg Lys Thr Ser Glu Arg Pro Gln	
45 50 55	
CCT CGT GGA AGG CGA CAA CCT ATC CCC AAG GCT CGC CAA CCC GAG GGT	2044
Pro Arg Gly Arg Arg Gln Pro Ile Pro Lys Ala Arg Gln Pro Glu Gly	
60 65 70	
AGG GCC TGG GCT CAG CCC GGG TAC CCT TGG CCC CTC TAT GGC AAT GAG	2092
Arg Ala Trp Ala Gln Pro Gly Tyr Pro Trp Pro Leu Tyr Gly Asn Glu	
75 80 85	
GGC TTG GGG TGG GCA GGA TGG CTC CTG TCA CCC CGC GGC TCC CGG CCT	2140
Gly Leu Gly Trp Ala Gly Trp Leu Leu Ser Pro Arg Gly Ser Arg Pro	
90 95 100 105	
AGT TGG GGC CCC ACG GAC CCC CGG CGT AGG TCG CGT AAT TTG GGT AAG	2188
Ser Trp Gly Pro Thr Asp Pro Arg Arg Arg Ser Arg Asn Leu Gly Lys	
110 115 120	
GTC ATC GAT ACC CTC ACA TGC GGC TTC GCC GAC CTC ATG GGG TAC ATT	2236
Val Ile Asp Thr Leu Thr Cys Gly Phe Ala Asp Leu Met Gly Tyr Ile	
125 130 135	
CCG CTC GTC GGC GCC CCC CTA GGG GGC GCT GCC AGG GCT CTA GCG CAT	2284
Pro Leu Val Gly Ala Pro Leu Gly Gly Ala Ala Arg Ala Leu Ala His	
140 145 150	
GGC GTC CGG GTT CTG GAG GAC GGC GTG AAC TAT GCA ACA GGG AAT CTG	2332
Gly Val Arg Val Leu Glu Asp Gly Val Asn Tyr Ala Thr Gly Asn Leu	
155 160 165	

- 246 -

CCT	GGT	TGC	TCC	TTT	TCT	ATC	TTC	CTT	TTG	GCT	TTG	CTG	TCC	TGT	TTG	2380
Pro	Gly	Cys	Ser	Phe	Ser	Ile	Phe	Leu	Leu	Ala	Leu	Leu	Ser	Cys	Leu	
170					175					180					185	
ACC	ATC	CCA	GCT	TCC	GGG	ATC	CAA	ATG	GAA	GAC	GCC	AAA	AAC	ATA	AAG	2428
Thr	Ile	Pro	Ala	Ser	Gly	Ile	Gln	Met	Glu	Asp	Ala	Lys	Asn	Ile	Lys	
				190					195					200		
AAA	GGC	CCG	GCG	CCA	TTC	TAT	CCT	CTA	GAG	GAT	GGA	ACC	GCT	GGA	GAG	2476
Lys	Gly	Pro	Ala	Pro	Phe	Tyr	Pro	Leu	Glu	Asp	Gly	Thr	Ala	Gly	Glu	
		205						210					215			
CAA	CTG	CAT	AAG	GCT	ATG	AAG	AGA	TAC	GCC	CTG	GTT	CCT	GGA	ACA	ATT	2524
Gln	Leu	His	Lys	Ala	Met	Lys	Arg	Tyr	Ala	Leu	Val	Pro	Gly	Thr	Ile	
		220					225					230				
GCT	TTT	ACA	GAT	GCA	CAT	ATC	GAG	GTG	AAC	ATC	ACG	TAC	GCG	GAA	TAC	2572
Ala	Phe	Thr	Asp	Ala	His	Ile	Glu	Val	Asn	Ile	Thr	Tyr	Ala	Glu	Tyr	
	235					240					245					
TTC	GAA	ATG	TCC	GTT	CGG	TTG	GCA	GAA	GCT	ATG	AAA	CGA	TAT	GGG	CTG	2620
Phe	Glu	Met	Ser	Val	Arg	Leu	Ala	Glu	Ala	Met	Lys	Arg	Tyr	Gly	Leu	
250					255					260					265	
AAT	ACA	AAT	CAC	AGA	ATC	GTC	GTA	TGC	AGT	GAA	AAC	TCT	CTT	CAA	TTC	2668
Asn	Thr	Asn	His	Arg	Ile	Val	Val	Cys	Ser	Glu	Asn	Ser	Leu	Gln	Phe	
				270					275					280		
TTT	ATG	CCG	GTG	TTG	GGC	GCG	TTA	TTT	ATC	GGA	GTT	GCA	GTT	GCG	CCC	2716
Phe	Met	Pro	Val	Leu	Gly	Ala	Leu	Phe	Ile	Gly	Val	Ala	Val	Ala	Pro	
				285					290					295		

GCG AAC GAC ATT TAT AAT GAA CGT GAA TTG CTC AAC AGT ATG AAC ATT	2764
Ala Asn Asp Ile Tyr Asn Glu Arg Glu Leu Leu Asn Ser Met Asn Ile	
300 305 310	
TCG CAG CCT ACC GTA GTG TTT GTT TCC AAA AAG GGG TTG CAA AAA ATT	2812
Ser Gln Pro Thr Val Val Phe Val Ser Lys Lys Gly Leu Gln Lys Ile	
315 320 325	
TTG AAC GTG CAA AAA AAA TTA CCA ATA ATC CAG AAA ATT ATT ATC ATG	2860
Leu Asn Val Gln Lys Lys Leu Pro Ile Ile Gln Lys Ile Ile Ile Met	
330 335 340 345	
GAT TCT AAA ACG GAT TAC CAG GGA TTT CAG TCG ATG TAC ACG TTC GTC	2908
Asp Ser Lys Thr Asp Tyr Gln Gly Phe Gln Ser Met Tyr Thr Phe Val	
350 355 360	
ACA TCT CAT CTA CCT CCC GGT TTT AAT GAA TAC GAT TTT GTA CCA GAG	2956
Thr Ser His Leu Pro Pro Gly Phe Asn Glu Tyr Asp Phe Val Pro Glu	
365 370 375	
TCC TTT GAT CGT GAC AAA ACA ATT GCA CTG ATA ATG AAT TCC TCT GGA	3004
Ser Phe Asp Arg Asp Lys Thr Ile Ala Leu Ile Met Asn Ser Ser Gly	
380 385 390	
TCT ACT GGG TTA CCT AAG GGT GTG GCC CTT CCG CAT AGA ACT GCC TGC	3052
Ser Thr Gly Leu Pro Lys Gly Val Ala Leu Pro His Arg Thr Ala Cys	
395 400 405	
GTC AGA TTC TCG CAT GCC AGA GAT CCT ATT TTT GGC AAT CAA ATC ATT	3100
Val Arg Phe Ser His Ala Arg Asp Pro Ile Phe Gly Asn Gln Ile Ile	
410 415 420 425	

CCG GAT ACT GCG ATT TTA AGT GTT GTT CCA TTC CAT CAC GGT TTT GGA	3148
Pro Asp Thr Ala Ile Leu Ser Val Val Pro Phe His His Gly Phe Gly	
430 435 440	
ATG TTT ACT ACA CTC GGA TAT TTG ATA TGT GGA TTT CGA GTC GTC TTA	3196
Met Phe Thr Thr Leu Gly Tyr Leu Ile Cys Gly Phe Arg Val Val Leu	
445 450 455	
ATG TAT AGA TTT GAA GAA GAG CTG TTT TTA CGA TCC CTT CAG GAT TAC	3244
Met Tyr Arg Phe Glu Glu Glu Leu Phe Leu Arg Ser Leu Gln Asp Tyr	
460 465 470	
AAA ATT CAA AGT GCG TTG CTA GTA CCA ACC CTA TTT TCA TTC TTC GCC	3292
Lys Ile Gln Ser Ala Leu Leu Val Pro Thr Leu Phe Ser Phe Phe Ala	
475 480 485	
AAA AGC ACT CTG ATT GAC AAA TAC GAT TTA TCT AAT TTA CAC GAA ATT	3340
Lys Ser Thr Leu Ile Asp Lys Tyr Asp Leu Ser Asn Leu His Glu Ile	
490 495 500 505	
GCT TCT GGG GGC GCA CCT CTT TCG AAA GAA GTC GGG GAA GCG GTT GCA	3388
Ala Ser Gly Gly Ala Pro Leu Ser Lys Glu Val Gly Glu Ala Val Ala	
510 515 520	
AAA CGC TTC CAT CTT CCA GGG ATA CGA CAA GGA TAT GGG CTC ACT GAG	3436
Lys Arg Phe His Leu Pro Gly Ile Arg Gln Gly Tyr Gly Leu Thr Glu	
525 530 535	
ACT ACA TCA GCT ATT CTG ATT ACA CCC GAG GGG GAT GAT AAA CCG GGC	3484
Thr Thr Ser Ala Ile Leu Ile Thr Pro Glu Gly Asp Asp Lys Pro Gly	
540 545 550	

GCG	GTC	GGT	AAA	GTT	GTT	CCA	TTT	TTT	GAA	GCG	AAG	GTT	GTG	GAT	CTG	3532
Ala	Val	Gly	Lys	Val	Val	Pro	Phe	Phe	Glu	Ala	Lys	Val	Val	Asp	Leu	
555						560					565					
GAT	ACC	GGG	AAA	ACG	CTG	GGC	GTT	AAT	CAG	AGA	GGC	GAA	TTA	TGT	GTC	3580
Asp	Thr	Gly	Lys	Thr	Leu	Gly	Val	Asn	Gln	Arg	Gly	Glu	Leu	Cys	Val	
570					575				580					585		
AGA	GGA	CCT	ATG	ATT	ATG	TCC	GGT	TAT	GTG	AAC	AAT	CCG	GAA	GCG	ACC	3628
Arg	Gly	Pro	Met	Ile	Met	Ser	Gly	Tyr	Val	Asn	Asn	Pro	Glu	Ala	Thr	
				590				595					600			
AAC	GCC	TTG	ATT	GAC	AAG	GAT	GGA	TGG	CTA	CAT	TCT	GGA	GAC	ATA	GCT	3676
Asn	Ala	Leu	Ile	Asp	Lys	Asp	Gly	Trp	Leu	His	Ser	Gly	Asp	Ile	Ala	
			605					610					615			
TAC	TGG	GAC	GAA	GAC	GAA	CAC	TTC	TTC	ATA	GTT	GAC	CTC	TTG	AAG	TCT	3724
Tyr	Trp	Asp	Glu	Asp	Glu	His	Phe	Phe	Ile	Val	Asp	Leu	Leu	Lys	Ser	
		620					625				630					
TTA	ATT	AAA	TAC	AAA	GGA	TAT	CAG	GTG	GCC	CCC	GCT	GAA	TTG	GAA	TCG	3772
Leu	Ile	Lys	Tyr	Lys	Gly	Tyr	Gln	Val	Ala	Pro	Ala	Glu	Leu	Glu	Ser	
	635					640					645					
ATA	TTG	TTA	CAA	CAC	CCC	AAC	ATC	TTC	GAC	GCG	GGC	GTG	GCA	GGT	CTT	3820
Ile	Leu	Leu	Gln	His	Pro	Asn	Ile	Phe	Asp	Ala	Gly	Val	Ala	Gly	Leu	
650					655				660					665		
CCC	GAC	GAT	GAC	GCC	GGT	GAA	CTT	CCC	GCC	GCC	GTT	GTT	GTT	TTG	GAG	3868
Pro	Asp	Asp	Asp	Ala	Gly	Glu	Leu	Pro	Ala	Ala	Val	Val	Val	Leu	Glu	
				670				675					680			

CAC GGA AAG ACG ATG ACG GAA AAA GAG ATC GTG GAT TAC GTG GCC AGT	3916
His Gly Lys Thr Met Thr Glu Lys Glu Ile Val Asp Tyr Val Ala Ser	
685 690 695	
CAA GTA ACA ACC GCG AAA AAG TTG CGC GGA GGA GTT GTG TTT GTG GAC	3964
Gln Val Thr Thr Ala Lys Lys Leu Arg Gly Gly Val Val Phe Val Asp	
700 705 710	
GAA GTA CCG AAA GGT CTT ACC GGA AAA CTC GAC GCA AGA AAA ATC AGA	4012
Glu Val Pro Lys Gly Leu Thr Gly Lys Leu Asp Ala Arg Lys Ile Arg	
715 720 725	
GAG ATC CTC ATA AAG GCC AAG AAG GGC GGA AAG TCC AAA TTG TAA AAT	4060
Glu Ile Leu Ile Lys Ala Lys Lys Gly Gly Lys Ser Lys Leu Stop	
730 735 740	
GTAAGTGTAT TCAGCGATGA CGAAATTCTT AGCTATTGTA ATCCTCCGAG GCCTCGAGGT	4120
CGACGAATTC CGACTCCGGA ACCAATTACT GATAATGTAG AAGATCATAC AGACACCGTC	4180
ACATACACTA GCTAGTGATA GCATTAATAC AGTAAGTGCA TCATCTGGAG AATCCACAAC	4240
AGACGAGACT CCGGAACCAA TTACTGATAA AGAAGAAGAT CATAAGTCA CAGACACTGT	4300
CTCATACACT ACAGTAAGTA CATCATCTGG AATTGTCACT ACTAAATCAA CCACCGATGA	4360
TGCGGATCTT TATGATACGT ACAATGATAA TGATACAGTA CCACCAACTA CTGTAGGCGG	4420
TAGTACAACC TCTATTAGCA ATTATAAAAC CAAGGACTTT GTAGAAATAT TTGGTATTAC	4480
CGCATTAATT ATATTGTCCG CCGTGGCAAT ATTCTGTATT ACATATTATA TATATAATAA	4540
ACGTTACCGT AAATACAAAA CAGAGAACAA AGCTAGATT TTTGACTTAC ATAAATGTCT	4600
GGGATAGTAA AATCTATCAT ATTGAGCGGA CCATCTGGTT CAGGAAAGAC AGCCATAGCC	4660
AAAAGACTAT GGAATATAT TTGGATTTGT GGTGTCCCAT ACCACTAGAT TTCCTCGTCC	4720
TATGGAACGA GAAGGTGTCG ATTACCATTA CGTTAACAGA GAGGCCATCT GGAAGGGAAT	4780
AGCCGCCGGA AACTTTCTAG AACATACTGA GTTTTATAGGA AATATTTACG GAACTTCTAA	4840

2104649

- 251 -

AACTGCTGTG AATACAGCGG CTATTAATAA TCGTATTTGT GTGATGGATC TAAACATCGA 4900
TGGCGTTAGA AGTCTTAAAA ATACGTACCT AATGCCTTAC TCGGTGTATA TAAGACCTAC 4960
CTCTCTTAAA ATGGTTGAGA CCAAGCT 4987

We claim:

1. An antisense compound having a sequence complementary to a base sequence which consists of 10-34 bases and is extracted from:

5 (i) 93 bases from thymine at position 107 to adenine at position 199,

(ii) 152 bases from adenine at position 250 to cytosine at position 401, or

10 (iii) 52 bases from cytosine at position 808 to adenine at position 859,

of the base sequence shown in SEQ ID NO: 1.

2. An antisense compound according to claim 1 characterized in that said base sequence is extracted from:

15 (iv) 54 bases from guanine at position 127 to guanine at position 180,

(v) 34 bases from adenine at position 284 to thymine at position 317, or

(vi) 34 bases from cytosine at position 343 to cytosine at position 376.

20 3. An antisense compound according to claim 1 characterized in that said base sequence contains 8 bases from cytosine at position 830 to guanine at position 837.

4. An antisense compound according to claim 1 characterized in that said base sequence is selected from:

(1) a base sequence which is included within 54 bases from guanine at position 127 to guanine at position 180, and which contains 16 bases from cytosine at position 131 to adenine at position 146, 7 bases from cytosine at position 147 to cytosine at position 153, 6 bases from cytosine at position 151 to cytosine at position 156, or 6 bases from cytosine at position 175 to guanine at position 180,

(2) a base sequence which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains 5 bases from guanine at position 285 to thymine at position 289, or 6 bases from thymine at position 309 to thymine at position 314, and

(3) a base sequence which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains 5 bases from guanine at position 355 to adenine at position 359, or 5 bases from adenine at position 369 to guanine at position 373.

5. An antisense compound according to claim 4 characterized in that said base sequence is selected from:

(4) a base sequence consisting of 16-24 bases which is included within 24 bases from guanine at position 127 to cytosine at position 150, and which contains at least 16 bases from cytosine at position 131 to adenine at position 146,

(5) a base sequence consisting of 15-30 bases which is included within 49 bases from guanine at position 127 to cytosine at position 175, and which contains at least 7 bases from cytosine at position 147 to cytosine at position 153,

(6) a base sequence consisting of 15-30 bases which is included within 31 bases from cytosine at position 150 to guanine at position 180, and which contains at least 6 bases from cytosine at position 151 to cytosine at position 156,

(7) a base sequence consisting of 15-30 bases which is included within 31 bases from cytosine at position 150 to guanine at position 180, and which contains at least 6 bases from cytosine at position 175 to guanine at position 180,

(8) a base sequence consisting of 15-33 bases which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains at least 5 bases from guanine at position 285 to thymine at position 289,

(9) a base sequence consisting of 15-33 bases which is included within 34 bases from adenine at position 284 to thymine at position 317, and which contains at least 6 bases from thymine at position 309 to thymine at position 314,

(10) a base sequence consisting of 15-30 bases which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains at least 5 bases from guanine at position 355 to adenine at position 359,

(11) a base sequence consisting of 15-30 bases which is included within 34 bases from cytosine at position 343 to cytosine at position 376, and which contains at least 5 bases from adenine at position 369 to guanine at position 373.

(12) a base sequence consisting of 15-26 bases which is included within 26 bases from thymine at position 351 to cytosine at position 376, and which contains at least 5 bases from guanine at position 355 to adenine at position 359, and

(13) a base sequence consisting of 15-26 bases which is included within 26 bases from thymine at position 351 to cytosine at position 376, and which contains at least 5 bases from adenine at position 369 to guanine at position 373.

6. An antisense compound according to claim 5 characterized in that said base sequence consists of 15-20 bases and is extracted from the 20 bases from cytosine at position 139 to guanine at position 158.

7. An antisense compound according to claim 5 characterized in that said base sequence is represented by the 30 bases from cytosine at position 151 to guanine at position 180.

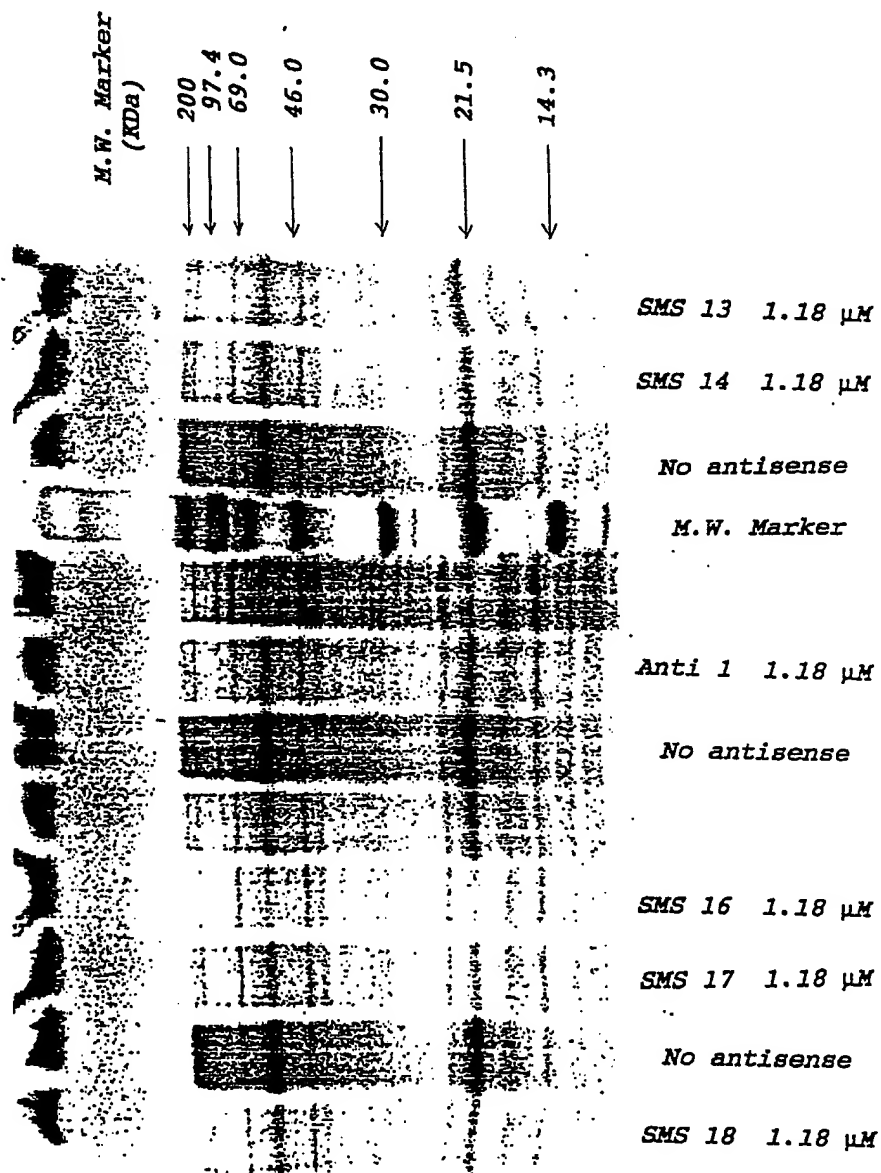
5 8. An antisense compound according to claim 5 characterized in that said base sequence is represented by the 20 bases from cytosine at position 131 to cytosine at position 150.

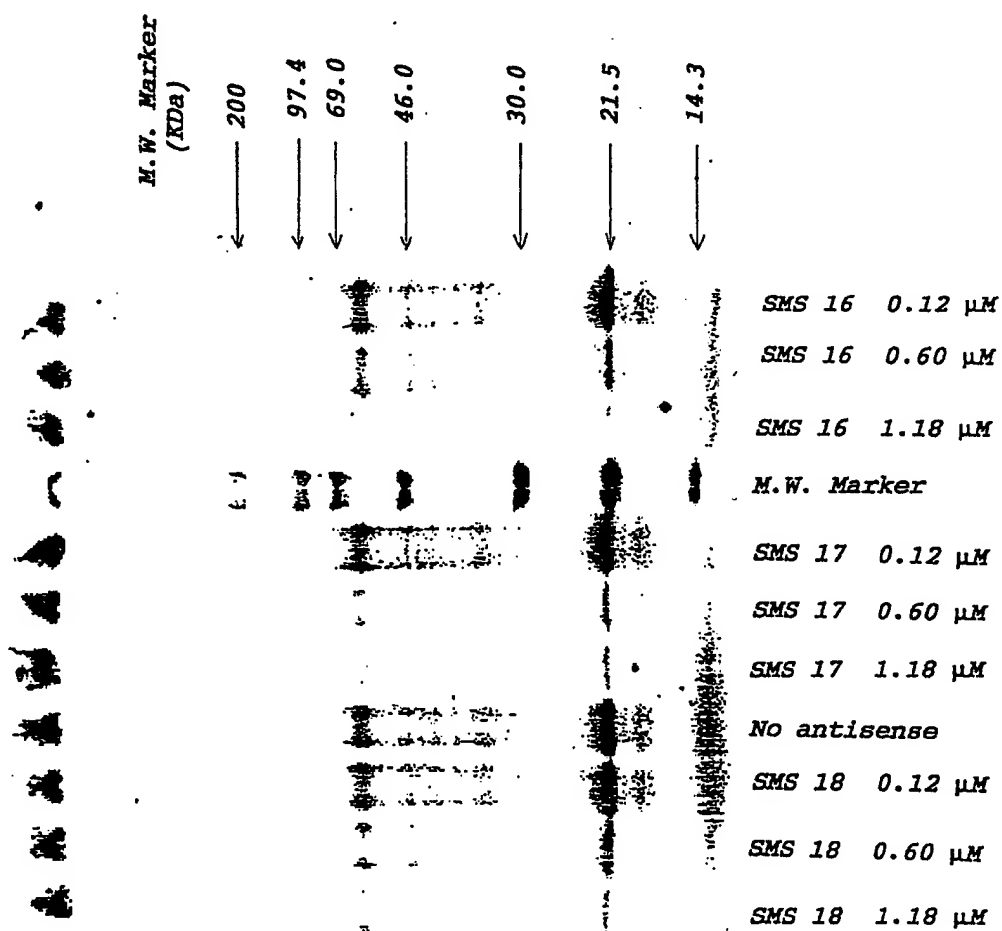
10 9. An antisense compound according to claim 5 characterized in that said base sequence is represented by the 19 bases from cytosine at position 141 to guanine at position 159.

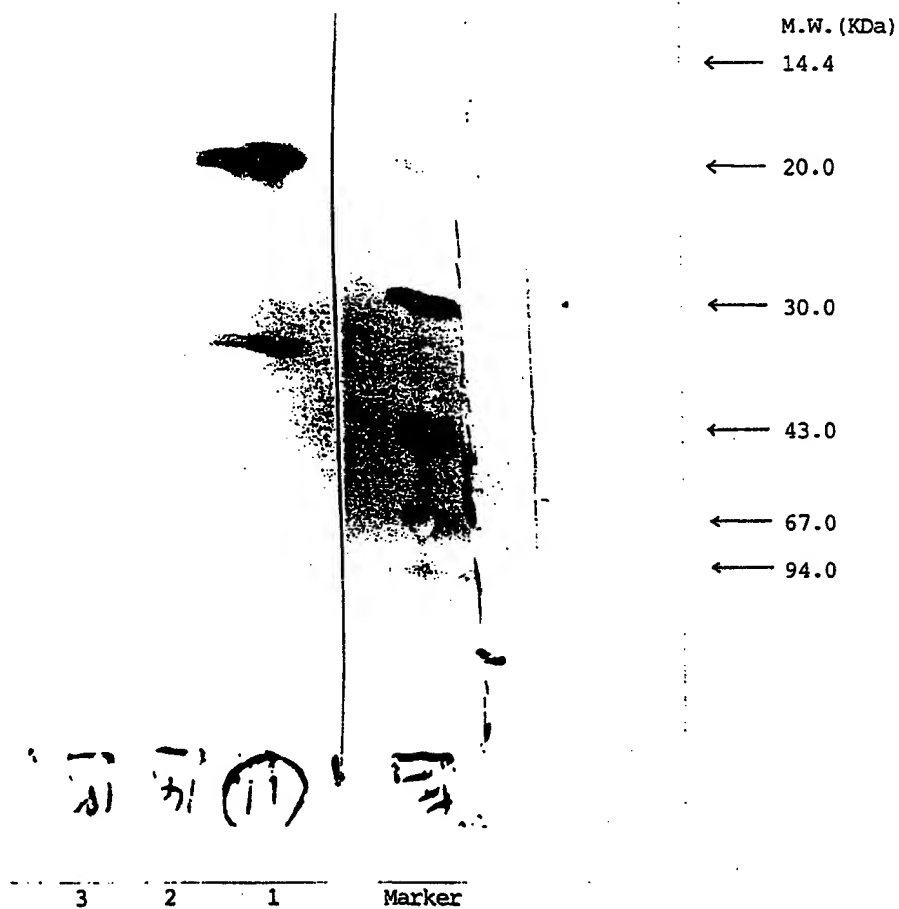
15 10. An antisense compound according to claim 5 characterized in that said base sequence is represented by the 20 bases from guanine at position 355 to cytosine at position 374.

20 11. An antisense compound according to claim 5 characterized in that said base sequence is represented by the 20 bases from thymine at position 353 to adenine at position 372.

12. An anti-hepatitis virus C formulation which comprises as an active ingredient an antisense compound according to claim 1.







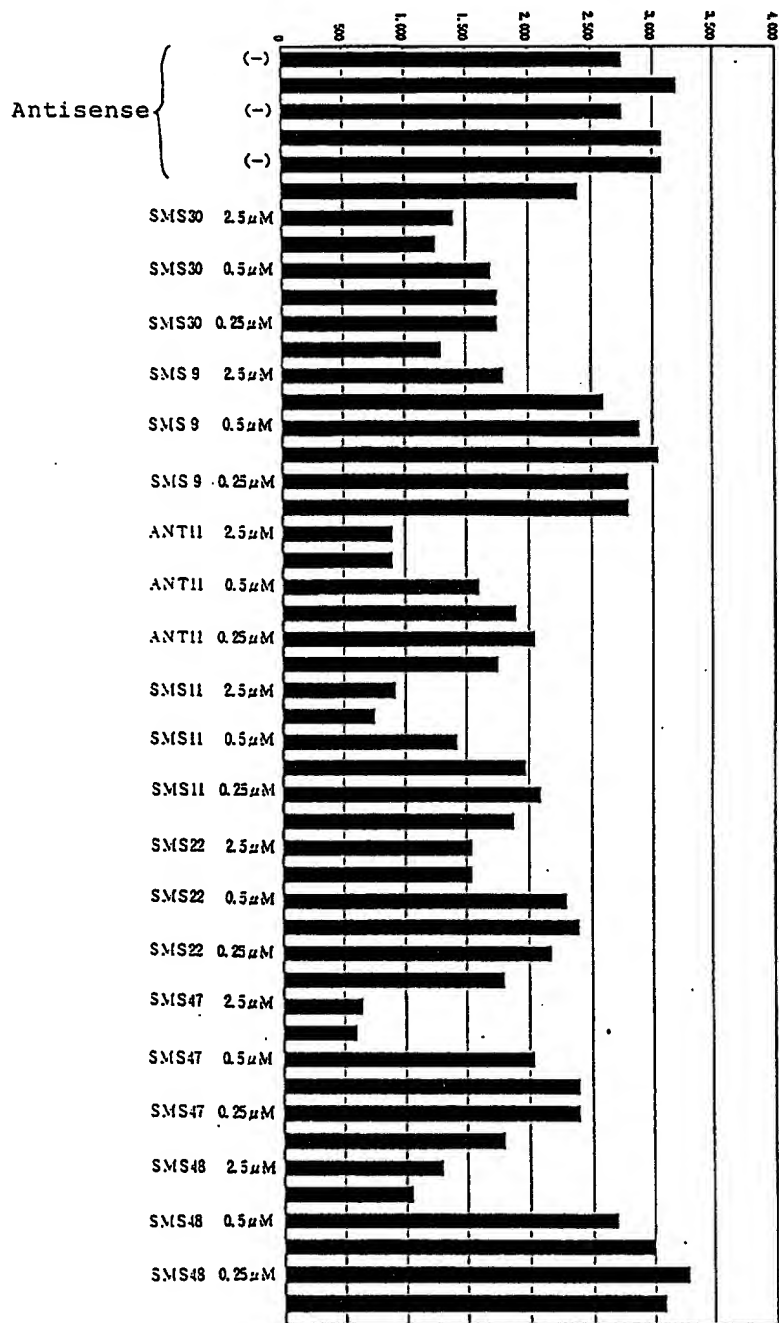
1. Recombinant Vaccinia Virus rVV5CL

2. Wild Type Vaccinia Virus

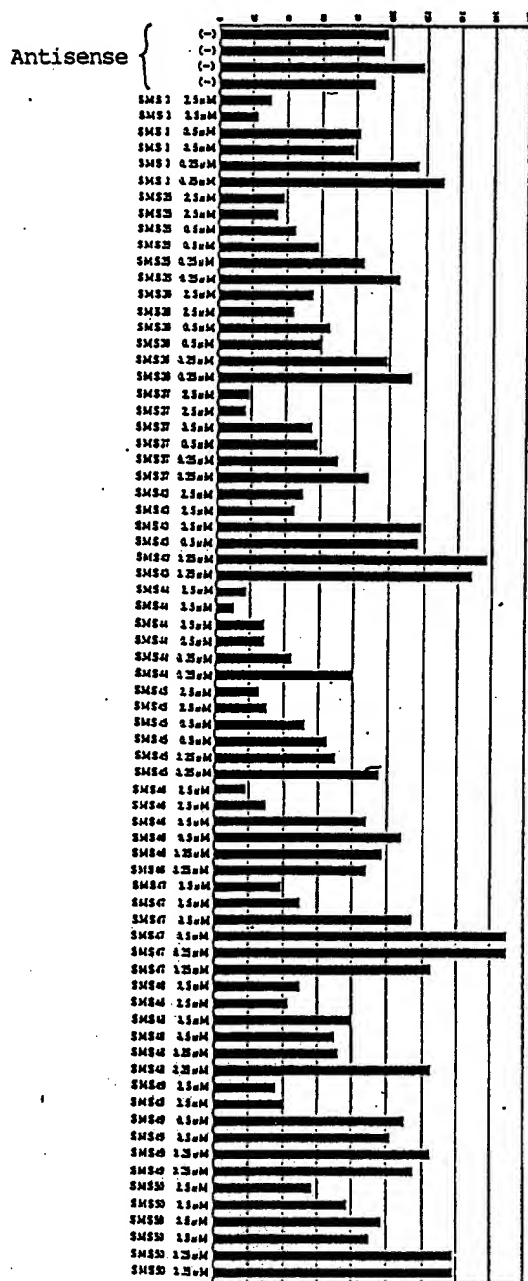
3. Wild Type Vaccinia Virus

Kirby, Eades, Gale, Baker

Fig. 4

*Kirby, Eades, Gale, Baker*

2104649



Kirby, Eades, Gale, Baker

2104649

